A CLINICAL AND ECONOMIC EVALUATION OF MEDICATION REVIEWS CONDUCTED BY PHARMACISTS FOR COMMUNITY-DWELLING AUSTRALIANS

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Volume One

Statements and Declarations

Declaration of Originality

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The research associated with this thesis abides by the international and Australian codes on human and animal experimentation, the guidelines by the Australian Government's Office of the Gene Technology Regulator and the rulings of the Safety, Ethics and Institutional Biosafety Committees of the University.

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"There is no such thing as absolute value in this world. You can only estimate what a thing is worth to you."

Charles Dudley Warner (1829-1900)
American essayist and novelist

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I'd imagine that virtually everyone who has seen a PhD through to completion would appreciate that it's not a solo effort, and I'm definitely no exception. Without the support, guidance, friendship and love (where appropriate) of the following people, I'm certain that this document would have never been completed:

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List of Publications

Peer-reviewed journal publications

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Conference abstracts (oral)

Stafford A. The top ten interventions in HMRs: What works and what doesn't? AACP's 6th annual consultant pharmacy clinical seminar, 29-31 May 2010, The Hotel Grand Chancellor, Hobart, Tasmania.

Stafford A, Tenni P, Peterson G, Doran C, Kelly W. The economic value of Home Medicines Reviews. Pharmacy Practice Research Summit 2010, 2-4 March 2010, Rydges Lakeside, Canberra, Australian Capital Territory, pp. 19.

Stafford A, Tenni P, Peterson G, Doran C, Kelly W. Home Medicines Reviews - what are the most valuable interventions? Working together to bridge the gaps in disease management. 3-4 September 2010, Grand Hyatt, Melbourne, Victoria, pp. 32-33.

Stafford A, Tenni P, Peterson G. The VALMER study (the Value of Medication Reviews) - what are common drug-related problems, and how do pharmacists resolve them? AACPs 5th annual consultant pharmacy clinical seminar, 28-31 May 2009, Sanctuary Cove, Queensland.

Conference abstracts (poster)

Stafford A, Tenni P, Peterson G, Doran C, Kelly W. Home Medications Reviews: The most common drug-related problems. Pharmacy Practice Research Summit 2010, 2-4 March 2010, Rydges Lakeside, Canberra, Australian Capital Territory, pp. 19.

Stafford A, Tenni P, Peterson G, Doran C, Kelly W. Home Medicines Reviews - what are the most common drug-related problems? Out of the Wilderness - 2009 APSA Annual

Conference, 9-11 December 2009, Wrest Point Convention Centre, Hobart, Tasmania, pp. 167.

Abbreviations

AACP	Australian Association of Consultant Pharmacy	MAI	Medication Appropriateness Index
ABDI	Australian Burden of Disease and Injury	MBS	Medicare Benefits Schedule
ACE	Angiotensin Converting Enzyme	MCQ	Multiple-Choice Question
ADE	Adverse Drug Event	MCS	Microscopy Culture and Sensitivity
ADR	Adverse Drug Reaction	MDC	Major Diagnostic Criteria
ALOS	Average Length of Stay	MMA	Medicare Modernisation Act
AR-DRG	Australian Refined Diagnosis Related Group	MMR	Medication Management Review
ASCEPT	Australasian Society of Clinical and Experimental Pharmacologists and Toxicologists	MRP	Medication-Related Problems
ATC	Anatomic Therapeutic Chemical	MTM	Medication Therapy Management
BCPS	Certification as a Pharmacotherapy Specialist	MTP	Medication-Therapy Problems
BEACH	Bettering the Evaluation and Care of Health	MUR	Medicines Use Reviews
CBA	Cost-Benefit Analysis	NHS	National Health Service
CCA	Cost-Consequence Analysis	NICE	National Institute for Clinical Excellence
CEA	Cost-Effectiveness Analysis	NPS	National Prescribing Service
CEAC	Cost-Effectiveness Acceptability Curve	NSAID	Non-Steroidal Anti-Inflammatory Drugs
CGP	Certification as a Geriatric Pharmacy Specialist	PBS	Pharmaceutical Benefits Scheme
CI	Clinical Intervention	PCI	Pharmaceutical Care Issues
CMA	Cost Minimisation Analysis	PhARIA	Pharmacy Accessibility/Remoteness Index of Australia
CMPMMP	Community Pharmacy Medicines Management Project	PRN	When-Required
COX	Cyclo-oxygenase	PSA	Probabilistic Sensitivity Analysis
CUA	Cost-Utility Analysis	PTO	Person Trade-Off
DAA	Dosage Administration Aid	QALY	Quality-Adjusted Life-Years
DALY	Disability-Adjusted Life-Year	QOL	Quality of Life
DMMR	Domiciliary Medication Management Review	QUM	Quality Use of Medicines
DRP	Drug-Related Problem	QUMCIT	Quality Use of Medicines In The Community Implementation Trial
DTP	Drug-Therapy Problems	RACF	Residential Aged Care Facility
DVA	Australian Government Department of Veterans' Affairs	RCT	Randomised Controlled Trial
EQ-5D	EuroQOL-5D	RMMR	Residential Medication Management Review
GBD	Global Burden of Disease	SF-36	Short-Form 36 Health Survey
GDP	Gross Domestic Product	SG	Standard Gamble
GP	General Practitioner	SHPA	Society of Hospital Pharmacists of Australia
HMG-CoA	Hydroxymethylglutamyl-Coenzyme A Reductase	SMART	Seniors Medication Assessment Research Trial
HOMER	Home-Based Medication Review Study	TTO	Time Trade-Off
ICER	Incremental Cost-Effectiveness Ratio	UK	United Kingdom
ICPC2-PLUS	International Classification of Primary Care Version 2 Plus	USA	United States of America

IMSANZ	Internal Medicine Society of Australian and New Zealand	VALMER	The Value of Medication Reviews Study
INR	International Normalised Ratio	WHO	World Health Organisation
IQR	Interquartile Range	WHO-CHOICE	World Health Organisation Choosing Interventions That Are Cost-Effective

Abstract

Introduction: There is a high prevalence of drug-related problems (DRPs) in community-dwelling residents which results in increased morbidity, mortality and healthcare expenditure. The Australian government has reimbursed pharmacists to identify and prevent or resolve DRPs through Home Medicines Reviews (HMRs) in these patients since 2001. Funding for the HMR program was based on studies undertaken prior to its implementation that indicated HMRs would be cost-effective due to reductions in drug costs and health service utilisation. Since the introduction of the program, there has been limited Australian research into the economic outcomes of HMRs. Furthermore, the results of international studies have questioned the clinical and cost-effectiveness of pharmacist-led medication reviews. The overall aim of the research described in this thesis was to investigate the clinical and cost-effectiveness of HMRs. To achieve this aim, the following objectives were formulated and addressed:

- to investigate novel methods for assessing the clinical and cost-effectiveness of HMRs;
- to investigate the characteristics of the DRPs identified in HMRs, including the drugs and conditions involved, and the recommendations made to resolve or prevent DRPs;
- to estimate the clinical effectiveness and cost-effectiveness of HMRs; and
- to investigate potential avenues to optimise the clinical effectiveness and cost-effectiveness of HMRs.

Method: A methodology that used expert opinion to predict the outcomes of HMRs was developed, based on previous research of interventions undertaken in community pharmacies. The development of this methodology necessitated two studies to be undertaken whereby the healthcare system costs and quality of life effects of numerous common clinical conditions resulting from medication use were estimated using a combination of expert opinion and literature values.

To evaluate HMRs, an observational cohort study was conducted across all states in Australia. Pharmacists accredited to perform HMRs submitted a random sample of HMRs that they had undertaken in 2008. Information from the HMR referral, report

and outcomes of the HMR were classified according to standardised systems and entered into an electronic database for analysis. A panel of experts reviewed a sample of the HMRs and estimated the clinical outcomes of the recommendations made in the HMRs. A cost-consequence and cost-utility analysis was performed to evaluate the cost-effectiveness of HMRs from an Australian government perspective.

A sub-study was undertaken that investigated the relationship between cost-effective HMRs and factors that prior research suggested may influence the cost-effectiveness of HMRs.

Results: A "consequences table" was developed whereby estimates of healthcare system costs and quality of life effects of 51 common clinical consequences were evaluated at three levels of severity. The estimates of these parameters appeared to be plausible and reasonable, and demonstrated moderate to high validity and reliability where testing was possible.

Six hundred and sixty-one HMRs were submitted by one hundred and forty-nine pharmacists. The HMR reports documented 2323 DRPs, of which the most common were *Condition not adequately treated* (16.5% of DRPs), *Therapy required* (11.3%) and *Toxicity evident* (10.6%). The most common DRP was inadequate pain management which was identified in 118 (17.9%) patients. The drug groups most commonly involved in DRPs were antithrombotics, peptic ulcer and oesophageal reflux therapies, and lipid modifying agents.

The pharmacists made 2727 recommendations to resolve the DRPs. The most frequently made recommendations included performing laboratory monitoring, commencing a new medication, or ceasing another. Information relating to the outcomes of the recommendations made to resolve the DRPs was available for 66% of the data (1801 recommendations). Of these recommendations, 1565 (87%) required the prescriber to act on the recommendations to implement them. Approximately three quarters of the DRPs documented in the HMRs were potentially resolved or managed.

On average, each HMR was estimated to result in a saving to the health system of $85.79, which was insufficient to offset the cost of the HMR ($323.80). Savings

resulted from predicted reductions in health resource utilisation (general practitioner and specialist visits, medical investigations and hospitalisations (P<0.001)). A trend in reduced drug costs was also observed (P=0.070). Significant reductions in the risk of arrhythmias, confusion and myopathy were predicted to occur as a result of the HMRs (P<0.001). Quality of life was estimated to improve minimally (0.001 QALYs per patient, P<0.001), and the cost per QALY gained (incremental cost-effectiveness ratio) was $177 566. Extensive sensitivity analysis was undertaken, which indicated minimal likelihood that HMRs were cost-effective using a threshold of $50 000 per QALY. A majority of the potential savings to the healthcare system occurred in a small number of HMRs.

A sub-study of the factors associated with cost-effective HMRs identified that the pharmacists who had performed cost-effective HMRs had undertaken more continuing-education (P=0.006) and performed more HMRs in total (P=0.041) than the pharmacists who had not performed cost-effective HMRs. A greater proportion of HMR referrals that contained recent and relevant pathology/ laboratory data resulted in cost-effective HMRs compared to referrals that did not (P=0.03).

Limitations resulting primarily from the methodology employed to assess the HMRs may have resulted in the study underestimating the cost-effectiveness of HMRs. Had a longer time horizon than 12-months been used, then greater cost savings to the healthcare system and improvements in quality of life would have been realised. The inclusion of other costs to the healthcare system not considered in the study also may have resulted in HMRs demonstrating greater cost-effectiveness.

Conclusion: DRPs are frequently identified and reported in HMRs. However, the economic and clinical benefits of addressing most of them are minor in the 12 months following the HMR. Future research should focus on the identification of predictors of cost-effective HMRs and increasing the uptake of HMRs using these factors if funding for the program is to continue.

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Overview

The need for medication reviews

The cost of medications in developed nations accounts for a large and growing proportion of healthcare expenditure. In Australia, approximately AU$113 billion was spent on healthcare in the twelve months between July 2008 and June 2009, equating to 9.0% of gross domestic product (GDP).[1] Of this, $15.2 billion was spent on medications, an increase of 9.6% over the previous year. Owing primarily to the ageing of the population, this trend is expected to continue - government spending on health is predicted to increase by approximately 75% by the year 2050.[2]

To ensure that this spending achieves optimal health outcomes in a cost-effective manner, the Council of Australian Governments formulated Australia's National Medicines Policy in 1999.[3] A central objective of this policy is the National Strategy for Quality Use of Medicines (QUM).[4] QUM is defined according to three tenets:[5]

1. Wise selection of management options, which involves:
    - consideration of the role of medication in treating illness and maintaining health, and
    - recognition of non-drug strategies to manage many disorders;
2. Choosing suitable medications if medication is deemed necessary through consideration of:
    - the patient's preferences, their clinical condition and co-existing conditions,
    - the risks and benefits of therapy,
    - dosage and duration of treatment,
    - monitoring considerations, and
    - costs to the patient, the community and health system as a whole; and
3. Safe and effective use of medications via:
    - monitoring of outcomes,
    - minimisation of misuse, over-use and under-use, and
    - improving people's ability to resolve issues related to medication, such as adverse effects.

The need for the national QUM strategy became increasingly apparent through the 1980s and 1990s.[6] Whilst medications are prescribed to ultimately improve health and health outcomes, this is not always the case. A high prevalence of medication-related illness in the community (such as adverse drug events, ADEs) has been documented in numerous studies. The 2009 National Prescribing Service (NPS) report *Medication Safety in the Community : A Review of the Literature* identified that 5.6% of general hospital admissions (equating to an estimated 190 000 admissions annually[7]) in Australia result from ADEs.[8] This was a considerable increase from a 2002 estimate of 140 000 admissions per year.[9]

Elderly patients appear to be particularly vulnerable to ADEs. One study in Tasmania, Australia, reported that 30.4% of unplanned hospital admissions in patients aged >75 years resulted from ADEs.[10] Furthermore, Burgess *et al.* found that the rate of ADE-related hospitalisation in Western Australians aged >60 years had increased substantially between 1980 and 2002.[11] The burden of ADEs on healthcare resources is not limited to hospitalisations - international studies have identified that ADEs are responsible for up to 33.2% of emergency department visits, and between 0.3% and 0.4% of general practitioner (GP) visits.[8]

The financial costs associated with managing ADEs are considerable. In 1995, it was estimated that cost of medication-related illness in the United States of America (USA) exceeded USD$76 billion.[12] By the year 2000, it was estimated that this had increased to over USD$177 billion, of which over 70% resulted from hospital admissions (approximately USD$121 billion).[13] There are no directly comparable Australian data, however it has been estimated that hospitalisation costs alone are AU$660 million,[7] a considerable increase from the 2002 estimate of AU$380 million.[9]

Whilst there will always be a level of unavoidable risk of harm associated with medication use, a substantial proportion of these admissions are considered to be avoidable. In a review of studies investigating the prevalence of drug-related hospital admissions in Australia, Roughead *et al.* reported that between 32% and 69% of these admissions were definitely or possibly preventable, had appropriate prior measures been taken by health workers.[14] Consequently, there has been considerable interest in interventions that may reduce the incidence of ADEs and health expenditure. A number of research projects were funded by the Australian government through QUM

Evaluation Programs in the 1990s to assess models of practice for healthcare professionals to improve medication use.[6]

Five of these projects investigated models of pharmacist-conducted medication management reviews (MMRs) for people living in their own homes. The interest in MMRs in this setting stemmed primarily from two federally-funded MMRs programs which commenced in the 1990s. The first of these was through the Australian Government Department of Veterans Affairs (DVA), which commenced funding for pharmacists to undertake MMRs for eligible veterans and their widows in 1994.[15] Subsequently, federal government funding for MMRs for all residential aged-care facility (RACF) residents began in 1997 (termed the Residential Medication Management Review, or RMMR, program).[16]

A detailed overview of each of the five MMR-related QUM Evaluation Program projects for community-dwelling patients is presented in Section 1.3.1 of Chapter One of this thesis. In general, each project demonstrated that MMRs for community-dwelling patients were likely to improve patient outcomes and potentially reduce healthcare expenditure. Consequently, federal funding for the HMR program (also referred to as Domiciliary Medication Management Review or DMMR) commenced in October 2001. This funding was initially provisioned in the Third Community Pharmacy Agreement between the Commonwealth of Australia and the Pharmacy Guild of Australia, and concluded in 2005.[15] These funding arrangements were renewed in the Fourth Agreement (2005-2010)[17] and subsequently the Fifth Agreement, which commenced in 2010.[18]

The HMR program has involved a substantial investment on behalf of the Commonwealth government. The funding for HMRs budgeted in the Third Community Pharmacy Agreement involved $43.4 million for GPs and pharmacist services, which was increased to $54.15 million in the Fourth Agreement, and maintained at this level in the Fifth Agreement ($52.11 million). In addition to the costs of undertaking HMRs, the Third Agreement provisioned $19.5 million for the role of MMR facilitators to promote the HMR and RMMR programs.[15] A further $29 million was allocated to the facilitator program in the Fourth Agreement; however, the facilitator program was not

continued into the Fifth Agreement.[17] As at August 2011, pharmacies are reimbursed up to $194.07[19] and GPs $143.40[20] for their involvement in a HMR.[i]

In terms of numbers of HMRs that have been performed, as at September 2010, GPs had claimed for participation in over 275 000 HMRs since the program's inception (Figure 1).[21] Equivalent data for pharmacies is only available to the end of 2008, and at this time they had been reimbursed for approximately 225 000 HMRs.[22]

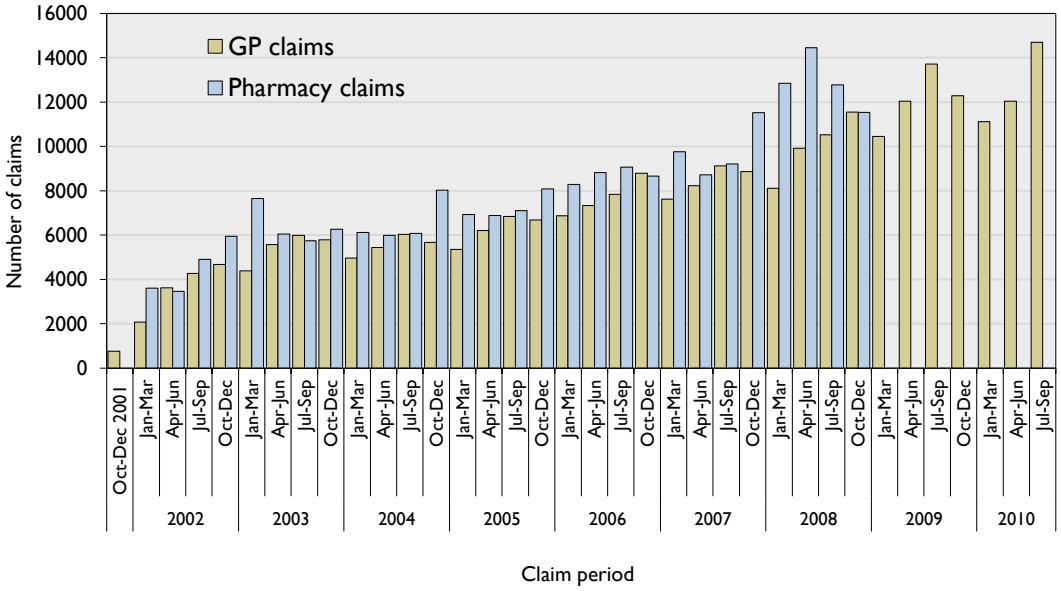

FIGURE 1 - NUMBER OF HMRS CLAIMED BY GPS AND PHARMACIES SINCE OCTOBER 2001 (PHARMACY DATA UNAVAILABLE FOR 2009 ONWARDS). SOURCE: MEDICARE AUSTRALIA[21] AND PHARMACY GUILD OF AUSTRALIA[22]

Despite the results of the Australian QUM Evaluation projects, more recent international literature regarding the outcomes of similar MMR programs has not been as positive. Chapter One of this thesis discusses in detail several large, controlled studies of MMR that have failed to demonstrate any tangible clinical benefits or improvements in QOL resulting from the intervention. Furthermore, several of these studies did not identify that pharmacist-conducted MMRs were cost-effective,[23-25] and

[i] Prior to October 2011, only community pharmacies, and not individual pharmacists, were reimbursed for HMRs.[19]

one study associated MMRs with increasing the likelihood of hospitalisation by 30% over usual care in patients at high risk of ADEs.[26]

Since the implementation of the HMR program, there has not been a large investigation into its effectiveness or cost-effectiveness. Most of the recent Australian research has focussed on evaluating the outcomes of MMRs conducted for specific patient populations,[27, 28] or quantified outcomes such as DRPs, which do not readily translate into clinical or economic benefits.[29] Furthermore, in 2009 a qualitative research project reported that consumers who had received HMRs found them *"'nice but not really necessary' as they did not believe it had made a significant difference to their health"*.[30] The report also commented that the effect of HMRs in *"reducing adverse drug events associated with polypharmacy was reported to be rare"*.

The sustained escalation in health expenditure has resulted in many countries adopting policies to identify health care services that offer comparatively less benefit in terms of overall health gain and cost-effectiveness.[31] Termed "disinvestment", this process is intended to allow the reallocation of funding to interventions and programs that are more cost-effective. In the UK, the National Institute for Clinical Excellence (NICE) has adopted a formal policy agenda to, "purge from the NHS (National Health Service) treatments that do not improve health or are poor value for money".[32] The identification of ineffective and not cost-effective healthcare practices with the intention of disinvestment is clearly a priority for the Australian Government, as stated in the Intergenerational Report 2010:

> *"In light of these escalating health pressures, it will be important to ensure that the health system provides value for money. This requires a health system that responds well to innovation, funding cost-effective improvements to health care while being able to adjust spending levels in areas where better value for money could be obtained."* [2]

Whilst there is no evidence that the HMR program is not cost-effective, there is also a paucity of recent research into its cost-effectiveness. Consequently, it is possible that the program may become a target for disinvestment unless it is rigorously researched.

Aims of thesis

In the absence of evidence of the current effectiveness or cost-effectiveness of the HMR program, it is difficult to make any informed decision regarding its ongoing funding. The general aim of this thesis was to assess the clinical and cost-effectiveness of HMRs in Australia, and investigate potential avenues to optimise their effectiveness and cost-effectiveness. To achieve this aim, three studies were undertaken. The first two studies were undertaken to address methodological limitations present in prior research in the area so as to develop the methodology used in the final study, termed the VALMER study (the Value of Medication Reviews Study), in which the clinical and economic effectiveness of HMRs was evaluated.

This thesis commences with a review of the literature relevant to the development of medication reviews, followed by an overview of studies that evaluated their effectiveness and cost-effectiveness. Throughout this discussion, methodological considerations for conducting studies of this complex intervention are presented to illustrate the considerations involved in assessing medication reviews, in order to justify the final methodology used in the study.

Funding notes

This thesis describes aspects of a project assessing the economic value of the Home Medicines Review program (Project IIG-021). This project was funded by the Australian Government Department of Health and Ageing as part of the Fourth Community Pharmacy Agreement through the Fourth Community Pharmacy Agreement Grants Program managed by the Pharmacy Guild of Australia.

Statement of contribution

Except where explicitly stated otherwise, the author of this thesis was solely responsible for the collection, analysis and interpretation of the data contained within it.

Ethics approval

This project received approval from the Human Research Ethics Committee (Tasmania) Network (ethics reference H9360) prior to its commencement (Appendix I).

Chapter 1 - Background

1.1 Pharmaceutical care

1.1.1 History and definition

The potential role for pharmacists in improving health outcomes, such as the desirable outcomes of medication use, is not new. Pharmacists have provided clinical services in hospitals for several decades,[33] which have been demonstrated to improve care with no evidence of harm.[34] During this time, numerous economic evaluations of clinical pharmacy services have been undertaken, and several major reviews of these evaluations have concluded that clinical pharmacy services are cost-effective.[35-39]

The practice of clinical pharmacy involves pharmacists ensuring *"optimal safety in the distribution and use of medicine"*,[40] which is primarily a medication-focussed concept. "Pharmaceutical care" is a patient-focussed concept that was first described by Mikeal *et al.* over 30 years ago. They defined pharmaceutical care as "*the care that a given patient requires and receives which assures safe and rational drug use*".[41] Brodie *et al.* elaborated on this definition by asserting that pharmaceutical care involves the determination of both drug needs and also the services necessary (before, during and after treatment) to ensure optimally safe and effective therapy.[42] Hepler and Strand, in what is considered by many to be a milestone publication, then integrated the desirable outcomes of pharmaceutical care into its definition. They considered pharmaceutical care to be "*the responsible provision of drug therapy for the purpose of achieving definite outcomes that improve a patient's quality of life (QOL)*".[43] The outcomes they specified were:

- to cure a disease;
- to reduce or eliminate symptomatology;
- to arrest or slow a disease process; or
- to prevent disease or symptomatology.

In addition to defining the philosophy of pharmaceutical care, Hepler and Strand outlined the processes involved in achieving its desired outcomes. They described pharmaceutical care as *"the process through which a pharmacist cooperates with a*

patient and other health professionals in designing, implementing and monitoring a therapeutic plan that will produce specific therapeutic outcomes for the patient".[43] Hepler and Strand considered that the process of pharmaceutical care primarily involves:

- identifying potential and actual DRPs;
- resolving actual DRPs; and
- preventing potential DRPs.[43]

1.1.2 Drug-related problems

The core activity of pharmaceutical care involves identifying and addressing DRPs.[43] DRPs are referred to in the literature by a variety of terms. These include medication-related problems (MRPs),[44] drug therapy problems (DTPs),[45] medication-therapy problems (MTPs),[46] and pharmaceutical care issues (PCIs).[47] In addition to these different names, there is no singularly accepted definition of a DRP.[48] However, most definitions are similar and encompass the same concept, that being "*an event or circumstance involving a patient's drug treatment that actually, or potentially, interferes with the achievement of an optimal outcome*".[48]

Numerous systems that classify DRPs have been developed and used in research and practice applications. A review by van Mil *et al.* identified at least 14 different DRP classification systems that had been utilised in assessments of pharmaceutical care.[48] These are shown in Table 1. Subsequent to that review, several more classifications have been published, including those of Peterson and Tenni,[49, 50] Laaksonen *et al.*,[51] Doucette *et al.*[52] and Nguyen.[53]

TABLE 1 - DRP CLASSIFICATION SYSTEMS REVIEWED BY VAN MIL *ET AL*.[48]

• ABC	• ASHP Classification	• Cipolle / Morley / Strand
• Granada Consensus	• Hanlon	• Hepler / Strand
• Krska	• Mackie	• NCC-MERP
• PAS	• PCNE	• PI-Doc
• SHB-SEP	• Westerlund	

The lack of a standard classification system complicates direct comparisons between studies with regards to the prevalence of different DRP types. Furthermore, according to the definition outlined previously, a DRP may be *potential* (where there is latent risk but no apparent adverse consequence) or *actual* (whereby the patient actually experiences a sub-optimal outcome). Some DRP classification systems differentiate between actual and potential DRPs, and therefore some studies report only actual DRPs, whereas others report total numbers of DRPs.

Irrespective of these issues, the prevalence and characteristics of DRPs in community-dwelling patients has been extensively researched in multiple different patient cohorts in many countries. Depending upon the clinicians involved, criteria used to define a DRP, classification system used and populations studied, the mean number of DRPs identified in studies of community-dwelling residents taking medication ranged between 1.3 and 8.2 per patient, with most reporting between two and three. Table 2 presents a summary of selected studies that investigated the prevalence of DRPs in non-hospitalised patients during studies of pharmaceutical care-type interventions.

TABLE 2 - SUMMARY OF STUDIES INVESTIGATING PREVALENCE OF DRPS IDENTIFIED DURING PHARMACEUTICAL CARE-TYPE INTERVENTIONS PROVIDED FOR COMMUNITY-DWELLING PATIENTS

STUDY	POPULATION	CLINICIAN IDENTIFYING DRPS	SETTING FOR DRP IDENTIFICATION	PREVALENCE AND MOST COMMON TYPES OF DRPS IDENTIFIED
Alldred *et al.*[54]	331 nursing home residents in the UK	Single pharmacist	Medication review performed at care facility	≥1 DRP identified in 77% of patients Mean 2.3 DRPs per patient 49% of DRPs "test to monitor medicine" 13% of DRPs "stop medicine" 10% of DRPs "start medicine"
Bell *et al.* 2006[27]	49 home-dwelling patients with mental illness considered at risk of medication misadventure in Australia	11 pharmacists	Medication review performed at patient's residence or community pharmacy	Mean 8.2 DRPs per patient 25% of DRPs "adverse drug reactions" 7% of DRPs "potential interaction" 6% of DRPs "additional drug taken"
Castelino *et al.* 2010[55]	224 home-dwelling patients considered at risk of medication misadventure in Australia	Seven pharmacists	Medication review performed at patient's residence or community pharmacy	≥1 DRP identified in 98% of patients Mean 4.9 DRPs per patient 16% of DRPs "need for additional medicine" 14% of DRPs "investigation test required" 11% of DRPs "rationalisation of drug therapy"
Elliott and Thomson 1999[56]	128 nursing home residents in Australia	Two pharmacists	Medication review performed at care facility	Mean 2.0 DRPs per patient 27% of DRPs "inappropriate or suboptimal dose" 17% of DRPs "no indication" 13% of DRPs "inappropriate duration of therapy"

STUDY	POPULATION	CLINICIAN IDENTIFYING DRPS	SETTING FOR DRP IDENTIFICATION	PREVALENCE AND MOST COMMON TYPES OF DRPS IDENTIFIED
Ellitt *et al*. 2009[57]	76 home-dwelling patients considered at risk of medication misadventure recently discharged from hospital in Australia	Pharmacists (unspecified number)	Medication review performed at patient's residence or community pharmacy	≥1 DRP identified in 93% of patients Mean 5.6 DRPs per patient 32% of DRPs "uncertainty about aim of the drug" 22% of DRPs "interaction" 15% of DRPs "adverse reaction"
Krähenbühl *et al.* 2008[58]	125 home-dwelling patients with a six-month cost of drug therapy exceeding US$1440 in Switzerland	Initial review by a single pharmacist followed by assessment by two other pharmacists	Medication review performed at community pharmacy (patient not present)	≥1 DRP identified in 86% of patients Mean 2.6 DRPs per patient 21% of DRPs "drug-drug interactions" 20% of DRPs "adherence problems" 14% of DRPs "duplicate drugs"
Krska and Avery[59]	738 home-dwelling patients with cardiovascular disease in the UK	60 pharmacists	Medication review and follow up consultations performed at community pharmacy	≥1 DRP identified in 88.5% of patients Median 3 DRPs per patient 27% of DRPs "monitoring issues" 15% of DRPs "indication but no treatment" 10% of DRPs "lifestyle issues"
Pit *et al.* 2007[60]	142 home-dwelling patients identified using a "Medication Review Checklist" in New South Wales, Australia	11 general practitioners	Medication review performed during consultation	≥1 DRP identified in 88% of patients Mean 1.3 DRPs per patient 54% of patients "likely to experience ADE" 50% of patients "experiencing compliance problems"
Rao *et al.* 2007[61]	1598 home-dwelling patients aged ≥40 in Minnesota, USA	Pharmacists (unspecified number)	Pharmaceutical care delivered in community pharmacies or medical clinics	≥1 DRP identified in 77% of patients Mean 2.3 DRPs per patient 32% of DRPs "needs additional drug therapy" 23% of DRPs "dosage too low" 16% of DRPs "non-compliance"

STUDY	POPULATION	CLINICIAN IDENTIFYING DRPS	SETTING FOR DRP IDENTIFICATION	PREVALENCE AND MOST COMMON TYPES OF DRPS IDENTIFIED
Roughead *et al.* 2004[62]	1000 home-dwelling patients considered at risk of medication misadventure in South Australia	63 pharmacists	Medication review performed at patient's residence	≥1 DRP identified in 90% of patients Mean 2.2 DRPs per patient 33% of patients (17% of DRPs) "need additional test" 27% of patients (11% of DRPs) "using wrong or inappropriate medication" 25% of patients (12% of DRPs) "need additional medication"
Ruths *et al.* 2003[63]	1354 nursing home residents in Norway	4 member physician/ pharmacist panel	Medication review performed at care facility	≥1 DRP identified in 76% of patients Mean 1.8 DRPs per patient 26% of DRPs "risk of ADE" 20% of DRPs "choice of drug" 13% of DRPs "need additional drug"
Sellors *et al.* 2003[64]	431 patients aged ≥65 and taking ≥5 regular medications in Ontario, Canada	24 pharmacists	Medication review performed during consultation	≥1 DRP identified in 80% of patients Mean 2.5 DRPs per patient 28% of DRPs "not receiving required drug" 19% of DRPs "not taking an appropriate drug" 13% of DRPs "not taking a drug appropriately"
Sorensen *et al.* 2004[65-67]	176 home-dwelling patients considered at risk of medication misadventure in Australia	53 pharmacists	Medication review performed at patient's residence or community pharmacy	≥1 DRP identified in 100% of patients Mean 5.5 DRPs per patient 17% of DRPs "potential ADE" 16% of DRPs "sub-optimal monitoring" 13% of DRPs "label discrepancy/ other adherence issue"

STUDY	POPULATION	CLINICIAN IDENTIFYING DRPS	SETTING FOR DRP IDENTIFICATION	PREVALENCE AND MOST COMMON TYPES OF DRPS IDENTIFIED
Stafford *et al.* 2009[68]	Two cohorts in Australia: • 138 home-dwelling patients considered at risk of medication misadventure • 96 nursing home residents	200 pharmacists	Home-dwelling cohort: medication review performed at patient's residence or community pharmacy Nursing home cohort: medication review performed at care facility	Home-dwelling cohort: ≥1 DRP identified in 99% of patients Mean 4.8 DRPs per patient 24% of DRPs "drug selection issues" 19% of DRPs "toxicity or adverse effect" 17% of DRPs "untreated indication" Nursing home cohort: ≥1 DRP identified in 100% of patients Mean 3.9 DRPs per patient 26% of DRPs "drug selection issues" 21% of DRPs "toxicity or adverse effect" 14% of DRPs "untreated indication"
Vinks *et al.* 2006[69]	196 home-dwelling patients aged ≥65 and taking ≥6 regular medications in the Netherlands	Pharmacists (unspecified number)	Medication review performed at community pharmacy (patient not present)	≥1 DRP identified in 100% of patients Mean 3.9 DRPs per patient 24% of DRPs "no existing indication" 21% of DRPs "contraindication" 18% of DRPs "drug-drug interaction"

There are several noteworthy points from the data presented in this table. Firstly, it is apparent that DRPs are identified in the majority of patients investigated in studies of those considered to be at high risk of experiencing such issues. Secondly, there are some trends with regards to the types of DRPs most frequently identified. It is important to note that DRPs related to undertreatment are often the type of issue most commonly identified in these studies. This is consistent with the results of some broader studies that have investigated QUM in at-risk populations.[70, 71] There is also a high frequency of DRPs involving a lack of monitoring for drug efficacy or toxicity, which seems aligned with the goal of QUM of ensuring safe and effective medication use.

However, the identification of a DRP alone is insufficient to prevent the consequences associated with it - there also needs to be some action taken for the DRP to be resolved or managed. In pharmaceutical care, it is generally accepted that the pharmacist should be able to take appropriate action to resolve the DRP.[42] This may involve resolving the DRP themselves (for example, through patient education or counselling), or making recommendations to the patient's physician to alter the patient's therapy. Should the DRP require the physician's involvement to resolve (which is common as pharmacist prescribing is limited or absent in most countries), another layer of complexity is introduced as the physician may not concur with the DRP identified by the pharmacist and/or the recommendation made to resolve it.

This was investigated by Lau and Dolovich who systematically reviewed the DRPs and the recommendations made to resolve them in studies of pharmaceutical care.[72] They reported an overall implementation rate for the pharmacists' recommendations of 66%, with the highest implementation rates identified in the provision of patient education (81.6% of recommendations implemented) and initiation of preventative action (78.6%). In contrast, recommendations to change or cease drugs were less frequently accepted (46.3% and 57.7%, respectively).

Finally, clinical outcomes may not occur solely because a DRP has been resolved, nor may the resolution of some DRPs be expected to have any clinical impact.[73] For example, DRPs that are resolved by simplifying medication regimens or using equi-effective but less costly medications are unlikely to result in any clinically signifcant outcomes.

Based on the studies discussed thus far, it is apparent that pharmacists readily identify DRPs and make recommendations to resolve them during pharmaceutical care activities. Their recommendations are frequently implemented, resulting in changes to patients' medication management. Intuitively (and according to the very definition of pharmaceutical care), the identification and resolution of DRPs should improve patient outcomes. However, as discussed in the following section, clear clinical and economic benefits have not been demonstrated in several studies of pharmaceutical care, which has important implications for the Australian HMR model.

1.1.3 Clinical and economic outcomes of pharmaceutical care

In defining pharmaceutical care, Hepler and Strand did not restrict the practice to one particular area. Indeed, they stated that "*the fundamental goals, processes, and relationships of pharmaceutical care exist regardless of practice setting*."[43] However, by defining pharmaceutical care in such broad terms, it has been interpreted and implemented by pharmacists and their representative bodies in several ways. Furthermore, as pharmacy practice may differ between countries, there are many different models of pharmaceutical care.

A variety of different terms have been used to describe the various models of pharmaceutical care. These include cognitive services, medication management, medication therapy management and medication review.[74] Regardless of nomenclature, for an intervention by a pharmacist to be considered to be pharmaceutical care, most authors consider that it must fulfil the following criteria:

- a one-to-one consultation between a patient and a pharmacist with a focus on managing health or resolving DRPs;
- development of a care-plan; and
- pharmacotherapy follow-up.[75]

Most models of pharmaceutical care have been trialled in community pharmacy practice.

1.1.3.1 Early literature

One of the earliest investigations into the outcomes of pharmaceutical care was conducted in the USA by Lipton *et al.* in the late 1980s.[45] Their RCT involved 706 patients aged 65 years and over who received either usual care or pharmaceutical care for three months, commencing upon hospital discharge. At follow-up, an expert panel assessed the appropriateness of a sample of control and intervention patients' prescription medications according to a pre-determined scoring system. The panel assessed the intervention patients as experiencing significant reductions in five out of seven categories of prescribing inappropriateness compared to the control patients. However, no investigation into any patient-centred outcome (such as QOL) was undertaken.

In a subsequent smaller RCT by Hanlon *et al*., QOL was assessed using the Medical Outcome Study Short Form Health Survey (SF-36[ii]).[76] This study investigated the effect of pharmaceutical care versus usual care for 208 veterans by a single clinic-based pharmacist in the USA. Unlike the study by Lipton *et al.* discussed above, participants had not recently been hospitalised, although all were ≥65 years of age and taking ≥5 regular medications. Other outcomes measured in this study were prescribing appropriateness according to the Medication Appropriateness Index[iii] (MAI)[80, 81] potential ADEs, self-reported patient compliance and knowledge, and satisfaction after 12 months. No economic analysis was performed. At follow-up, the only significant difference between the intervention and control groups was in MAI scores, where the scores had declined by 28% in the intervention group (showing improved medication appropriateness) and 5% in the control (P<0.001).

A larger RCT that investigated the effects of pharmaceutical care on QOL in high-risk veterans in the USA was performed by Malone *et al.*[82] In this study, 1054 veterans received either pharmaceutical care or usual care for a 12-month period. The

[ii] QOL measurement using tools such as SF-36 and EQ-5D is discussed in Section 4.2.1

[iii] MAI is similar to criteria that identify potentially inappropriate prescribing, such as Beers' criteria.[77-79] In contrast to Beers' criteria (which simply identifies potentially inappropriate drugs) MAI provides a score of the inappropriateness of each patient's medication regimen. A higher MAI score indicates a greater degree of inappropriateness, and therefore greater potential risk of ADEs

intervention was assessed from three perspectives: economic, QOL (using SF-36) and patient satisfaction with their primary health care providers. At follow-up, there were no significant differences between intervention and control patients in QOL or patient satisfaction.[82, 83] The economic analysis identified that total healthcare costs had increased in both groups at follow-up. However, the increase in the intervention group (including the cost of providing the service) was slightly less than that in the control group ($1020 versus $1313, respectively), although this did not reach statistical significance (*P*=0.06). Savings resulted from reduced clinic visit costs (despite an increase in the number of clinic visits) and laboratory tests.

Bernsten *et al.* conducted a large (2454 patients), randomised, controlled, longitudinal trial of pharmaceutical care in seven European countries.[84, 85] The outcomes assessed included QOL (using SF-36), number of hospitalisations and patient-reported disease control, which were measured at baseline, 6, 12 and 18 months. A cost-effectiveness analysis was undertaken; however, differing healthcare systems between countries limited the researchers' ability to assess the economic outcomes of the program. At follow-up, there were no significant differences overall between the control and intervention groups in any of the QOL dimensions, although minor differences were identified in some QOL domains in several countries. Furthermore, there were no significant differences between control and intervention patients with regards to hospitalisation or mean total cost per patient.

In Australia, March *et al.* developed and assessed a community pharmacy-based pharmaceutical care service in an uncontrolled study.[44] Two hundred and five patients from five pharmacies were enrolled in the study which involved patients consulting with pharmacists over an 11-month period. There was an average of 3.4 consultations per patient during this time, which is considerably more pharmacist involvement than in a HMR. A comprehensive cost-benefit analysis was undertaken that used expert opinion to predict the expected changes in health resource costs (GP visits, specialist visits, other health professional visits and hospitalisations) resulting from the intervention[iv]. The expected net annual costs savings per patient ranged between $40

[iv] this methodology was also used in a subsequent study of medication reviews by the same research group and is discussed in further detail in Section 1.3.1.4 of this chapter [86]

and $311 depending upon their pharmacy, although there was no significant change in medication costs.

Etemad and Hay investigated the cost-effectiveness of pharmaceutical care by modelling its potential effects.[87] Literature sources were used to estimate reductions in medication-related mortality and savings resulting from reduced hospitalisations, visits to emergency departments and GPs, and nursing home admissions. Using these estimates, their model indicated that pharmaceutical care would be highly cost-effective-the base case indicated a cost of US$2100 per life-year saved, which did not increase above US$14 000 during sensitivity analysis.[v]

An important consideration in interpreting the results of this study is that there were several major limitations to the data sources used. Firstly, the estimates of the effect of pharmaceutical care on costs were primarily the median of the results of several studies, and not derived from meta-analysis. Secondly, most of the studies used to derive these estimates did not directly measure the outcome for which their results were used in the economic model. For example, to calculate part of the effect on hospitalisations, the authors first estimated the percentage of medication-related hospitalisations resulting from inappropriate prescribing. They then estimated the decrease in inappropriate prescribing resulting from pharmaceutical care using literature sources, and assumed that pharmaceutical care would therefore decrease the total number of hospitalisations resulting from inappropriate prescribing by that proportion. However, this assumption is based on the premise that the resolution of every instance of inappropriate prescribing prevents hospitalisation. This assumption is incorrect - there is a substantial amount of literature that has investigated the relationship between prescribing appropriateness and adverse events without evidence of a strong relationship.[77, 88-94] Furthermore, as recognised by the authors, mortality estimates were derived from expert opinion or indirectly-measured data and are therefore of uncertain validity. Finally, the study did not account for different types of pharmaceutical care delivery, and assumed that any intervention described as pharmaceutical care would achieve equivalent outcomes to any other. This is contradictory to the results of a number of systematic reviews of pharmaceutical care

[v] Thresholds of cost-effectiveness are discussed in Section 1.4.3

that have found significant differences in outcomes depending upon the way in which pharmaceutical care was implemented and the patients to whom it was provided.[29, 95-97]

1.1.3.2 Systematic reviews and more recent pharmaceutical care literature

Roughead *et al.* systematically reviewed RCTs that investigated the outcomes of professional pharmacist services (including pharmaceutical care).[74, 96] They found that the strongest evidence of benefit involved patients with asthma or heart failure, where pharmaceutical care was found to improve signs and symptoms of asthma, and surrogate endpoints of blood pressure, cholesterol levels and glycosylated haemoglobin in patients with poorly controlled diabetes. Further benefits were identified in terms of prescribing appropriateness and patient knowledge and compliance, especially in patient groups with poor knowledge and compliance at baseline.

The review's findings in terms of clinical outcomes were less favourable, as it was reported that there was little evidence of pharmaceutical care benefitting QOL. Notably, this is contrary to the primary aim of pharmaceutical care which is "*achieving definite outcomes that improve a patient's quality of life*".[43] It was suggested that this may have resulted from the measurement tools being insensitive or inappropriate for the benefits conferred by pharmaceutical care. Furthermore, the review identified that few studies have included ADEs as an outcome measure, despite the focus of pharmaceutical care involving the resolution of DRPs. Consequently, Roughead *et al*. concluded that the most appropriate outcome measure for future studies should be DRPs or ADEs defined by explicit criteria and assessed by independent researchers.

These findings and recommendations were aligned with those made in a review by Hanlon *et al*. published around the same time.[29] The authors of this review also suggested that future studies should be conducted in patients with a specific health problem that is highly sensitive to medication optimisation, rather than a heterogeneous patient group. They also asserted that large-scale, multi-centre studies would be required to determine the impact of these interventions.

One specific patient group that has been investigated involves patients with cardiovascular disease. A prospective, controlled study undertaken by Lee *et al*.

reported that pharmaceutical care significantly increased medication adherence and persistence in a population of elderly veterans with coronary artery disease risk factors in the USA.[98] This was associated with a significant reduction in systolic blood pressure (*P*=0.04) at six-month follow-up. However, no differences in low-density lipoprotein levels were discerned, clinical outcomes were not investigated, and no investigation into the cost-effectiveness of the program was undertaken. More recently, Eussen *et al*. reported that a pharmaceutical care program in the Netherlands significantly improved adherence with statin medications at six months (hazard ratio for discontinuation 0.66, 95% CI 0.46 to 0.96).[99] However, at 12 months follow-up, the difference in discontinuation rates was no longer statistically significant.

In a small study, Taylor *et al.* identified a reduction in several outcomes, including hospitalisation, resulting from a pharmaceutical care intervention.[100] Sixty-nine patients in rural Alabama, USA, were randomised to receive either pharmaceutical care (33 patients) or usual care (36 patients) for a period of 12 months. All patients were recruited as they were considered to be at high risk of medication misadventure using criteria similar to those that identify patients for HMR. The intervention was delivered in regular scheduled GP visits, where the pharmacists interviewed patients, provided patient education and made therapeutic recommendations to the GPs to resolve any DRPs that were identified. The outcomes measured in this study were:

- clinical markers of disease management (blood pressure, glycosylated haemoglobin, international normalised ratio (INR) in patients taking warfarin, and cholesterol concentration);
- prescribing appropriateness using the MAI;
- self-reported compliance;
- medication knowledge;
- QOL using SF-36; and
- markers of medication misadventure (ADEs, all-cause hospitalisations and emergency department visits).

Cost data was not collected, and an economic analysis was not undertaken in this study.

At follow-up, there were significant differences between the intervention and control patients in several of the outcome measures. The proportion of patients at treatment

targets (Table 3) and medication knowledge was improved, and the number of hospitalisations and emergency department visits were reduced in the intervention group compared to control. MAI scores improved in all 10 domains evaluated in the intervention group but worsened in 5 domains in the control group. However, despite these differences between the two groups, no significant difference was identified in QOL, and self-reported compliance did not improve.

TABLE 3 - NUMBERS OF PATIENTS AT THERAPEUTIC TARGETS BEFORE AND AFTER PHARMACEUTICAL CARE. FROM TAYLOR *ET AL.*[100]

CONDITION	NUMBER (% OF TOTAL) PATIENTS AT TARGET LEVELS				*P*-VALUE AT FOLLOW-UP
	INTERVENTION		CONTROL		
	BASELINE	FOLLOW-UP	BASELINE	FOLLOW-UP	
Hypertension	3 (13%)	22 (92%)	9 (31%)	8 (28%)	0.001
Diabetes mellitus	3 (23%)	13 (100%)	9 (56%)	5 (31%)	0.001
Dyslipidaemia	2 (11%)	14 (74%)	3 (16%)	1 (5%)	0.001
Anticoagulation	1 (25%)	4 (100%)	3 (50%)	1 (17%)	0.048

These positive results were not replicated in a much larger RCT conducted in the UK. The Randomised Evaluation of Shared Prescribing for Elderly people in the Community over Time (RESPECT) trial assessed the effectiveness and cost-effectiveness of a pharmaceutical care service.[101-103] More than 700 patients aged ≥75 years and taking at least five regular medications were randomised to receive either usual care or 12 months of pharmaceutical care. Patients were followed-up at 3 months, 12 months, and 12 months following the cessation of pharmaceutical care. The primary outcome measure was the MAI score, with secondary measures of patient knowledge, compliance and concordance, GP-reported adverse events, and QOL (measured with SF-36 and EQ-5D). A cost-utility analysis was undertaken from the perspective of the UK National Health Service with comprehensive sensitivity and uncertainty analyses.[vi]

At follow-up, there were no statistically significant differences in any of the outcomes measured. With regard to the economic analysis, pharmaceutical care was estimated to cost an average of £192 per year more than usual care to yield a benefit of 0.019 QALYs

[vi] Sensitivity and uncertainty analyses are discussed in Sections 2.4.4 and 2.4.5 , respectively

per patient. The incremental cost-effectiveness ratio (ICER) was therefore £10 000 per QALY gained, with a probability of cost-effectiveness between 0.78 and 0.81 at thresholds of £20 000 and £30 000 respectively. It is interesting to note that the sensitivity analysis indicated that there was greater cost-effectiveness in younger patients on fewer drugs compared to older patients on more drugs (Table 4). This was due to a disproportionately greater cost of providing pharmaceutical care compared to QOL improvements in the older patients on more drugs.

TABLE 4 - MODELLED COSTS AND QALYS OVER 12 MONTHS RESULTING FROM PHARMACEUTICAL CARE FOR PATIENT TYPES AS SHOWN IN RESPECT TRIAL [101]

MODELLED EXPECTATION FOR AVERAGE PATIENT TYPE	AVERAGE DIFFERENCE		ICER (£/QALY)
	QALYs*	COSTS (£)	
75yo, 5 drugs	0.019	89	4 661
80yo, 7 drugs	0.016	155	9 515
85yo, 10 drugs	0.017	302	17 980
90yo, 15 drugs	0.020	703	35 185

* difference between intervention and control not significant

Rather than simply presume that the intervention was clinically ineffective, the authors attributed the equivocal findings of the study to difficulties in implementing pharmaceutical care.[102] They highlighted issues with pharmacists being unable to organise meetings with GPs and access medical records as adversely affecting the effectiveness of the intervention. Potentially, as these data were collected under study conditions, the real-world implementation of such interventions will be more affected by these issues, which may further limit their effectiveness and cost-effectiveness.

Another study that assessed the effect of pharmaceutical care on QOL was undertaken in New Zealand by Bryant *et al*.[104] In a randomised, controlled trial, they investigated the outcomes of pharmaceutical care provided at on QOL and medication appropriateness using SF-36 and MAI respectively. In contrast to the expected beneficial effect of pharmaceutical care on QOL, the study identified a significant reduction in QOL in the intervention group in the domains of emotional role (13.4 unit difference, P=0.024) and social functioning (7.7 unit difference, P=0.019). This was despite a significant improvement in MAI scores in the intervention group compared to controls (reduction in MAI score of 2.0 (P<0.001) versus 0.3 (P=0.86) respectively). The

authors suggested that the reduction in QOL resulted from the patients possessing an increased awareness of their medical conditions which negatively impacted upon their perception of their health.

1.1.3.3 Medication Therapy Management

In the USA, the 2003 Medicare Modernisation Act (MMA) mandated Medication Therapy Management (MTM) programs for patients with multiple chronic diseases who take multiple medications.[105] MTM describes a variety of methods (such as mailed letters and interventions delivered via telephone or face-to-face) that may be employed to improve the quality of medication use. Service providers may choose the method/s by which they deliver MTM services, although consensus definitions of ideal components of MTM have been developed by a variety of organisations.[106] To date, the majority of MTM services have been delivered by pharmacists via what is essentially pharmaceutical care.[105]

A 2009 review of the literature investigating the outcomes of MTM services concluded that there was limited evidence that the service was beneficial in clinical or economic terms.[106] This was despite some evidence that MTM services may improve prescribing appropriateness and patient medication knowledge. Subsequent to this review, several studies have associated MTM with benefiting patient outcomes. For example, a non-randomised controlled study found that patients who received MTM were less likely to die than non-recipients (adjusted odds-ratio 0.5, 95% CI 0.3 to 0.9). However, the MTM-recipients were more likely to be hospitalised (adjusted odds-ratio 1.4, 95% CI 1.1 to 2.0) and have increased medication costs (adjusted odds-ratio 1.4, 95% CI 1.1 to 1.9) compared to non-recipients.[107] A limitation to this study was that the hospitalisation rate at baseline was 41% greater in the control group compared to the intervention group, which may indicate that the control patients were generally sicker than the intervention group.

Another study compared drug costs in patients who received MTM services via face to face or telephone discussions, or educational mail-outs.[108] At the 12-month follow-up period, the mean monthly drug costs in patients who received face to face or telephone counselling decreased by US$40 and US$15, respectively, whilst the mean monthly drug cost in the mail-out group was unchanged. An uncontrolled study of a single

pharmacist providing MTM services for 53 patients in an assisted living facility found a net saving of US$1550 in medication costs after 184 days.[109] Pindolia *et al*. retrospectively evaluated clinical and economic outcomes of patients who received MTM services during 2006 and 2007.[110] Patients who received MTM services were 60% less likely to have experienced a gastrointestinal bleed (*P*=0.001) than patients who did not receive MTM. Whilst drug costs declined in both groups, the MTM-recipients demonstrated a greater reduction than non-recipients (17.2% versus 7.0%, *P*=0.001). However, as no formal economic evaluation was conducted, it was not possible to conclude from the study whether MTM services are cost-effective.

1.2 Medication Review

1.2.1 Definitions, types and objectives

In many of the studies discussed thus far, the term "medication review" is used frequently. Indeed, "medication review" is used synonymously for pharmaceutical care and MTM by some authors.[104, 110] This is because there is no single definition of a medication review, and depending upon the country, practice setting, and health professional involved, a medication review invariably involves different tasks with potentially different outcomes. For the purposes of this thesis, medication review is considered to be a specific form of pharmaceutical care to differentiate it from interventions.

In the United Kingdom (UK), the Task Force on Medicines Partnership and The National Collaborative Medicines Management Services Programme defined four levels of medication review in the 2002 publication *Room for Review*.[111] These levels were:

- Level 0 (Ad-hoc review)-an unstructured, opportunistic review, such as a simple clarification of a dosage of a medication.
- Level 1 (Prescription review)-assessment of the appropriateness of a patient's medication when presented for dispensing, usually without access to the patient's clinical notes.
- Level 2 (Treatment review)-review of medications with full access to the patient's clinical notes. The patient may or may not be present.

- Level 3 (Clinical medication review)-review of the appropriateness of a patient's medications in consideration of their medical conditions and preferences.

Whilst these levels of medication review were defined by researchers in the UK, it is notable that only levels Zero and One have been widely implemented there. The UK was one of the first countries in the world to introduce Level One reviews (termed Medication Use Review or MURs), which have also been implemented in New Zealand and will shortly be introduced in Australia.[112, 113] Level Three medication review has been described by some experts as the gold standard; however, it is also the most expensive in time and other resources, and may not always be necessary.[114] Consequently, there is limited availability of Level Three reviews in the UK, and indeed most developed nations. In contrast to the limited global implementation, the Australian HMR program provides widespread availability of federally funded Level Three medication reviews to home-dwelling residents.

The Pharmaceutical Society of Australia Domiciliary Medication Management Review Guidelines define a HMR as "*a structured and collaborative health care service provided to consumers in the community setting to ensure their medicine use is optimal and fully understood and that continuity of care is enhanced*" and that is undertaken to "*improve quality of life and health outcomes*".[115] These guidelines describe the aims of a HMR as follows:

- to contribute to optimising the therapeutic effectiveness and management of the consumer's medication regimen;
- to facilitate a cooperative working relationship between pharmacists and other members of the health care team in order to benefit health and well-being; and
- to provide a medication information resource for the consumer and health professionals involved.[115]

To achieve these aims, HMRs are undertaken in a structured process that involves several groups of health professionals involved in a patient's care. The HMR process is described in detail in the following section.

1.2.2 The Australian Home Medicines Review process

1.2.2.1 Overview

The current HMR model (Figure 2) was developed during several of the MMR-related QUM Evaluation Program projects conducted in the late 1990s. The HMR process involves the patient, their usual GP, their community pharmacy, an accredited pharmacist, and potentially carers and other health professionals involved in the patient's care.[116] Once a patient has been identified as potentially benefitting from a HMR (see Section 1.2.2.2 below), the process is initiated by the patient's GP who prepares a referral for a HMR and forwards it to the patient's nominated community pharmacy. Upon receipt of the referral, the community pharmacy liaises with a specially accredited pharmacist to perform the review. The accredited pharmacist then interviews the patient at a location of the patient's choice (typically the patient's home, although the model allows for other locations to be used). During the interview, the pharmacist may undertake a variety of tasks, such as:

- collect information about the patient, such as their:
    - medication management (usage and storage of medications and medical devices);
    - previous medications (and reason for cessation or alteration);
    - history of allergy, drug sensitivity or adverse drug reactions (ADRs);
- provide education and advice to the patient (or their carer) regarding medications or therapeutic devices; and
- identify and resolve barriers to compliance.[115]

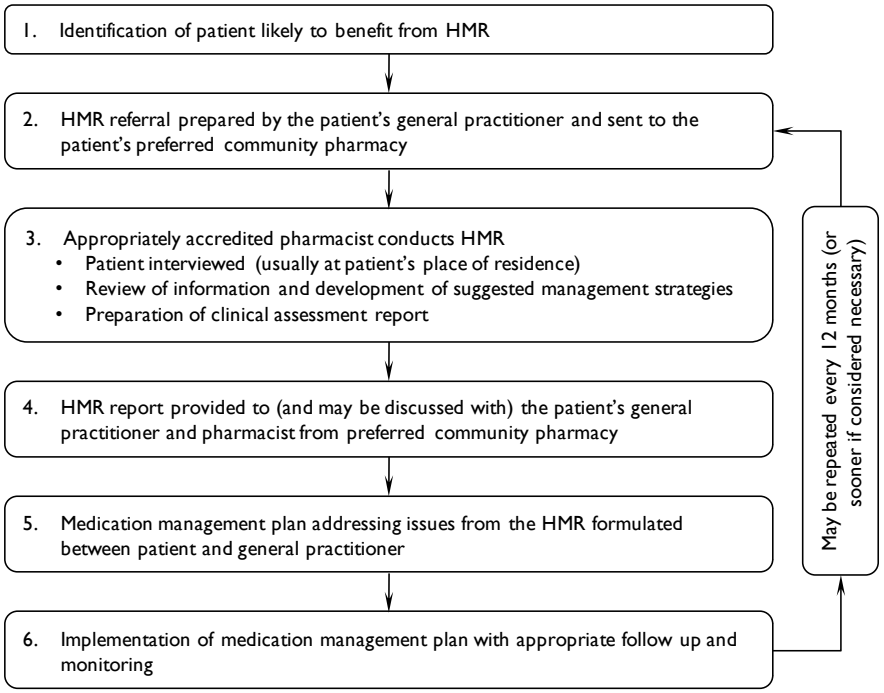

FIGURE 2 - FLOW DIAGRAM ILLUSTRATING CURRENT HMR PROCESS. MODIFIED FROM [116]

The reviewing pharmacist then evaluates all of the information they have collated regarding the patient to identify relevant DRPs and formulate a plan to resolve or prevent the DRPs. Based on this information, the pharmacist prepares a report for the referring GP that documents the DRPs and the recommendations made to address these DRPs. In consideration of the pharmacist's findings, the GP then formulates a medication management plan in consultation with the patient to implement any changes necessary to address the DRPs. Once implemented, the outcomes of the agreed management plan are monitored by the GP and the community pharmacy.

1.2.2.2 Patient eligibility and identification of potential recipients

Any Australian resident not hospitalised or residing in an aged-care facility is eligible for a HMR. Patients are only eligible for a single HMR every 12 months, unless there has been significant change to their medical status or medication profile. In such cases, a GP may refer a patient for a HMR within 12 months. Aside from these criteria, there are no further strict prerequisites that must be fulfilled for a patient to receive a HMR. Any person involved in a particular patient's care, such as a nurse, pharmacist, carer or

partner, may identify a potential HMR recipient. However, the patient's GP is currently the only provider who may generate a referral.

Whilst any home-dwelling Australian resident may receive a HMR, the Australian guidelines for the provision of HMR services specify several factors to assist in identifying patients at high risk of ADEs who may benefit from the service, shown in Table 5. These factors were generally based on the results of studies that associated them with an increased risk of ADEs. The prevalence and risk of medication misadventure associated with polypharmacy, commonly defined as patients taking five or more regular medications, has been researched by many authors.[117-123] For example, Hanlon *et al*. reported that 35% of veterans taking 5 or more medications had experienced at least one ADEs, 21% of which resulted in either hospitalisation or emergency care.[124] In a survey of residents of sheltered housing complexes (a level of care below that provided in nursing homes) in the UK, George *et al*. found that one or more medication-related risk factors was present in 72% of patients.[125] Unplanned hospitalisations and emergency department visits were associated with use of drugs of narrow therapeutic index (odds ratio (OR) 2.98, 95% CI 1.69 to 5.28, $P<0.001$), use of five or more medications (OR 2.10, 95% CI 1.34 to 3.31, $P=0.001$) and greater disability (OR 1.06, 95% CI 1.02 to 1.11, $P=0.005$).

TABLE 5 - SUGGESTED FACTORS TO ASSIST IN IDENTIFICATION OF PATIENTS MOST LIKELY TO BENEFIT FROM A HMR. MODIFIED FROM GILBERT *ET AL*.[126] AND SORENSEN *ET AL*.[66]

- Currently taking five or more regular medications
- Currently taking more than 12 doses of medications per day
- Significant changes made to medication treatment regimen in the last 3 months
- Medication with a narrow therapeutic index or requiring therapeutic monitoring
- Symptoms suggestive of an adverse drug reaction
- Sub-therapeutic response to treatment with medicines
- Suspected non-compliance or inability to manage medication-related therapeutic devices
- Having difficulty managing their own medicines because of literacy or language difficulties, dexterity problems or impaired sight, confusion/dementia or other cognitive difficulties
- Attending a number of different doctors, both general practitioners and specialists
- Recent (within the last four weeks) discharge from a facility / hospital

It is important to note that, as previously stated, it is not mandatory for a patient fulfil any of these criteria to receive a HMR. GPs may use their discretion in referring patients for a HMR where they consider it to be clinically appropriate.

The prevalence of these risk factors in patients who receive HMRs is not well characterised. Sorensen et *al*. reported on the interrelationships between medication-related risk factors in a randomised controlled trial of medication reviews.[67] In their study, the most frequently identified risk factors were confusion with generic and trade names (56% of patients) and poor adherence (52.5%). Possession of expired medications was most frequently related to other risk factors, followed by patients with therapeutic duplication and poor adherence.

Pit *et al*. investigated the prevalence of risk factors for medication misadventure amongst older people in general practice.[127] In their cohort of 849 patients aged >65 years, 54% were taking 5 or more medications, 59% had more than one doctor involved in their care, and 18 to 39% reported at least one potential ADE in the past month (dependent upon the type of ADE). In a sub-analysis of this data, GPs were significantly more likely to undertake medication reviews for patients with many of these risk factors compared to patients in whom the risks were not present (Table 6).[60]

TABLE 6 - FACTORS ASSOCIATED WITH ADES AND ODDS OF RECEIVING A MEDICATION REVIEW. ADAPTED FROM PIT *ET AL.*[60]

CHARACTERISTIC	NUMBER (%) OF PATIENTS		ODDS RATIO (95% CI)
	RECEIVED MMR	DID NOT RECEIVE MMR	
General			
3 or more health conditions	81 (77)	152 (48)	3.57 (1.70–7.49)
Poor health	38 (36)	48 (14)	3.52 (1.61–7.71)
>1 doctor involved in care	76 (69)	163 (49)	2.41 (1.32–4.37)
Lives alone	47 (43)	97 (33)	1.54 (1.00–2.38)
Patient had a fall in previous 12 months	31 (31)	50 (15)	2.59 (1.08–6.20)
Medication use			
5 medicines	94 (85)	134 (42)	7.69 (3.15–18.78)
Started new medicine in previous 4 weeks	26 (23)	52 (17)	1.48 (1.07–2.06)
Any medicines your doctor does not know about	9 (7)	6 (2)	4.46 (1.09–18.24)
Potential adverse drug reactions: Last month:			
Felt drowsy or dizzy	48 (50)	93 (29)	2.48 (1.36–4.49)
Felt nauseous	29 (29)	52 (15)	2.34 (1.11–4.92)
Had stomach problems	36 (34)	56 (17)	2.64 (1.49–4.67)
Compliance: For any drug used, do you have trouble with:			
Side effects	26 (27)	31 (10)	3.19 (1.88–5.39)
Knowing what your medicine is for	12 (12)	14 (4)	3.15 (1.21–8.22)
Reading the label	14 (16)	15 (4)	4.6 (1.29–16.44)
Opening bottles or packets	17 (18)	26 (8)	2.67 (1.07–6.68)
Sharing of medicines with others	1 (1)	1 (0)	2.9 (1.88–4.46)

Whilst these findings in terms of medication reviews undertaken by GPs, it is probable that the prevalence of these risk factors is similar in patients referred for HMRs.

1.2.2.3 Pharmacist accreditation

To be eligible to receive government reimbursement for undertaking HMRs and RMMRs, pharmacists must achieve and maintain a qualification additional to their licence to practice. Pharmacists must be accredited with either of two bodies responsible for training and assessing accredited pharmacists.[128] These two bodies are the Australian Association of Consultant Pharmacy (AACP) and Society of Hospital Pharmacists of Australia (SHPA). To obtain accreditation with either body, a pharmacist must have an undergraduate degree in pharmacy, be registered to practice

as a pharmacist in Australia, and successfully complete a variety of competency based assessments.[129, 130]

Pharmacists seeking accreditation with the AACP must undertake an initial training course (usually of two days duration, although some universities' undergraduate programs are now approved training courses).[129] Candidate pharmacists must then pass a 50 question multiple-choice question (MCQ) examination, maintain a portfolio demonstrating their competency to identify and resolve DRPs in their workplace, and finally complete four case study reviews to the satisfaction of a marker. Pharmacists accredited with the SHPA are required to have successfully completed the Certification as a Geriatric Pharmacy Specialist (CGP) or Certification as a Pharmacotherapy Specialist (BCPS) competency based assessments.[130] Despite being developed in the USA, these assessments involve a MCQ examination similar to parts of the AACP accreditation process.

Pharmacists accredited with AACP are required to reaccredit every year, and sit a reaccreditation examination every three years. Accredited pharmacists must annually provide evidence of their participation in a significant number of hours of continuing education activities and successfully complete an on-line MCQ examination. Pharmacists reaccrediting with SHPA must undertake a similar level of continuing education and maintain their CGP or BCPS qualification. As of 5 September 2011, there were 2086 pharmacists accredited with AACP,[131] and 54 pharmacists accredited with SHPA.[132]

1.2.2.4 Pharmacist and GP reimbursement

At the time of writing (August 2011), the current HMR model allows only the patient's community pharmacy and GP to claim for reimbursement for their involvement in the HMR process.[133] It is from the payment to the community pharmacy that the accredited pharmacist is paid, either as an employee or on a contractual basis. When the HMR program was introduced in 2001, the payment to the pharmacy was $140, whilst GPs received $128. These have increased in the subsequent decade, such that pharmacists are currently reimbursed $194.07[19] and GPs $143.40[20] for their involvement in each HMR.

Since 2005, an additional travel allowance has been available to the pharmacy for HMRs performed in remote areas of Australia, as defined by the Pharmacy Accessibility/Remoteness Index of Australia (PhARIA) categorisation.[134] Should the pharmacist travel a distance of 10km or greater (return trip) from the patient's residence, then they may claim an additional rural loading allowance, as shown in Table 7.

TABLE 7 - RURAL HMR TRAVEL LOADING ALLOWANCE FOR PHARMACIES ACCORDING TO PHARIA REMOTENESS CLASSIFICATION. ADAPTED FROM [19] AND [134]

PHARIA CATEGORY	REMOTENESS CLASSIFICATION	RURAL TRAVEL LOADING ALLOWANCE
1	Highly accessible	nil
2	Accessible (Group A)	$20
3	Accessible (Group B)	$30
4	Moderately accessible	$40
5	Remote	$50
6	Very remote	$60

To date, Medicare Australia has not released any data regarding the number of HMRs where the rural loading has been claimed. Consequently, the total cost of the HMR program is somewhat unknown (at least to the public).

1.3 Effectiveness and cost-effectiveness of HMRs

Having described the HMR process, it is now appropriate to review the literature involving the outcomes of HMRs. In general, an evaluation of any health care program involves the assessment of four different dimensions, namely:[135]

1. *Efficacy*: which investigates whether the intervention does more good than harm in people who fully comply with the associated recommendations or treatments;
2. *Effectiveness*: which evaluates whether the intervention does more good than harm in people to whom it is offered;
3. *Availability*: which assesses whether the intervention is accessible to all people who could benefit from it; and

4. *Cost-effectiveness*: whether the program is an efficient use of resources compared to other interventions that may achieve similar outcomes.

The focus of this thesis is the effectiveness and cost-effectiveness of HMRs, as a comprehensive evaluation of the availability of HMRs was undertaken in 2008.[30] Consequently, the following section provides an overview of the Australian and international studies that investigated the efficacy, effectiveness and/ or cost-effectiveness of medication reviews performed by pharmacists for patients living in their own homes. A focus is given to the methodology of each study, as each has aimed to capture different outcomes of this complex intervention. A review of Australian and international English language literature was undertaken by searching the following electronic databases:

- Pubmed Medline;
- Embase;
- International Pharmaceutical Abstracts;
- Cochrane Central Register of Controlled Trials;
- Cochrane Database of Systematic Reviews; and
- Informit Meditext.

The search strategy utilised free text searches with the following terms: 'medication review', 'pharmacist OR pharmacy or community pharmacist OR community pharmacy', 'pharmaceutical care', 'home medication review', 'medication management', 'community medication review', 'medication regimen review', 'Domiciliary Medication review', 'Domiciliary Medication management', 'general practice', 'primary care' and 'economic evaluation'. The bibliographies of the studies that were identified were hand searched for other relevant articles. The following websites were also searched: Pharmacy Guild of Australia, AACP, the Australian QUM map, UK NHS, and Department of Health and Ageing. All authors identified from the QUM map and authors of sentinel articles were used to develop an author search of the aforementioned databases.

An early conclusion from this literature review was that the majority of the published literature regarding the economic outcomes of pharmacist-conducted medication reviews has been undertaken in hospitalised patients or those residing in aged-care facilities.[35, 36, 38] Most studies involving community-dwelling patients focused on

quantifying outcome measures such as the identification and/or resolution of DRPs, or qualitative aspects of medication reviews. Although the identification, resolution and prevention of DRPs is a cornerstone of the medication review process, the relationship of DRPs to clinical outcomes resulting from their identification (such as ADRs, hospitalisation, or death) is not well established.[24] Consequently, the effects of medication reviews on costs and cost savings is also unclear. Given this uncertainty, the studies discussed in the next two sections of this chapter involved some assessment of patient centred-outcomes, rather than proxy measures such as DRPs and prescribing appropriateness.

1.3.1 Australian QUM Evaluation Program Projects

Each of the five MMR-related QUM Evaluation Program projects conducted in the 1990s attempted to provide some indication of the economic outcomes (and hence cost-effectiveness) of the medication reviews that were conducted. Only one study was of a randomised controlled design; two of the remaining projects used expert opinion to undertake cost-effectiveness analyses, and the remaining study only assessed drug costs before and after the intervention.

1.3.1.1 Clinical Pharmacist Review of Medication for the Elderly in a General Practice Setting (Greenhill 1996)

The earliest Australian study of medication reviews performed for home-dwelling residents was undertaken by Greenhill.[136] This uncontrolled study assessed the outcomes of medication reviews performed by a single pharmacist for 62 elderly patients in Western Australia. Six months after being reviewed by the pharmacist, each patient was assessed in terms of the following outcome measures, taken mainly from medical records:

- changes in number and cost of drugs;
- changes in daily doses taken and dose times;
- ADRs;
- GP visits;
- compliance;

- drug knowledge[vii]; and
- quality of life (using the Dartmouth COOP Functional Health Assessment charts).[137]

These data were used to perform a simple cost analysis; there was no consideration of the cost of providing the reviews.

Interpreting the results of this study is difficult, given the small sample size and poor documentation-the study was not published in peer-reviewed medical literature. The only documentation is a brief report (presumably to the funding body) with minimal description of the project methodology. In addition, limited statistical analysis of any of the measurements was performed. However, the findings are worthy of discussion as they provide some insight into subsequent research in the area.

Follow-up data was available for 53 patients, at which time the total annual drug cost saving was $4430, equating to an average saving of $83.58 per patient. However, no savings occurred in nine reviews and in the summary of findings in the project report the author excluded these nine patients. This resulted in the average saving per patient increasing to $100.68 per annum, although it is questionable whether this exclusion of patients where no changes occurred is appropriate as there still would have been a cost associated with providing the medication review.

The minimal documentation of the remaining outcomes limits the ability to interpret them. It is reported that there were no differences in the number of GP visits, medication taken, dose times or number of daily doses. The insignificant effect on GP visits suggests that the reviews would have resulted in minimal health care utilisation savings. The author commented that "subjective assessment" of compliance, drug knowledge and QOL showed positive changes, but it is not possible to interpret the data relating to these outcomes from the project report.

In addition to the flaws in report quality, analysis and interpretation, this study illustrates an important consideration when designing studies that assess the outcomes of medication reviews. An obvious limitation to Greenhill's study is the lack of a

[vii] the measurement tools for compliance and drug knowledge were not specified

comparator or control group. In the absence of such a comparator, attributing all of the benefits to the medication review alone is unreasonable as patient treatment may be altered for any number of other reasons (for example, medical specialist involvement or experiences with other patients). Indeed, Greenhill noted that recommendations made for one patient were then applied to other patients seen by the same GP without the pharmacist's making any recommendations regarding these patients.

1.3.1.2 Sutherland project (Krass *et al*. 1997-1999)

The second Australian study of pharmacist-conducted medication reviews for community- dwelling patients was "Medication regimen reviews: a collaborative project between pharmacists and general practitioners", known as the Sutherland project.[138-140] This study was conducted in several stages between 1995 and 1999, during which time 45 pharmacists completed medication reviews for a total of 275 patients in New South Wales. The stated aims of the final stage of the Sutherland project were to:

- implement a protocol for GPs to identify ambulatory patients for referral to community pharmacy for medication review; and
- evaluate the clinical significance and cost savings associated with the intervention.

There were two phases to this stage of the study. Phase one focussed primarily on achieving the first of these aims, whilst the economic and clinical evaluations were undertaken in the second phase. In both phases, patient follow-up occurred three months after the medication review. No QOL measurements were performed at any stage of the study; instead, the clinical significance of the medication changes occurring as a result of the reviews was rated by a panel of experts.

A partial cost-benefit analysis was undertaken using a combination of empirical and modelled data. The costs considered were drug costs, hospital costs, GP visits and specialist visits. As there was no control group in this study, the only empirical data collected were drug costs. The patients' drug regimens were costed at the time of the review and at follow-up. It was assumed that no changes would have occurred in the absence of the medication review. The remaining costs were estimated using expert

opinion. This involved a clinical pharmacist, a clinical pharmacologist, a GP and consultant physician who rated the interventions made in 141 reviews. For each review, each expert predicted the change in probability of an adverse outcome occurring as a result of the interventions made by the pharmacist in the medication review. The health care costs associated with the adverse outcomes were then estimated by the experts who predicted the course of treatment required to resolve each adverse event over a 12-month period.

Although not explicitly stated by the authors, the economic analysis was predominantly from the perspective of whoever was to pay for the reviews (which became the Australian government when HMR was implemented). The aim of the analysis was to investigate whether remuneration for pharmacists and GPs would be offset by reduced medication costs and health care utilisation. Remuneration was substantially less than current HMR levels: pharmacists were paid $100 per review, and GPs $50. The net total cost was therefore defined by Equation 1. A comprehensive sensitivity analysis that investigated several variables was undertaken as part of the analysis; however no uncertainty analysis was performed. As expert opinion is notoriously variable,[141] this is a major limitation to the economic analysis undertaken in this study.

EQUATION 1 - COST-BENEFIT ANALYSIS EQUATION USED IN THE SUTHERLAND PROJECT

$$\text{Net total cost} = \text{Cost of HMR} + \Delta \text{ Medication cost} + \Delta \text{ Healthcare costs}$$

Δ Medication cost = change in medication costs; Δ Healthcare costs = change in healthcare costs

The pharmacists made recommendations to modify the patients' drug therapy in over 80% of the medication reviews in this study, of which approximately 40% were enacted upon by the GP. The economic analysis identified that, on average, the cost of the medication review ($150) was totally offset by savings in drug cost and health resource utilisation ($372.43, Table 8). As is evident from the large inter-quartile ranges in each group, there was significant variability with regards to savings between individual reviews.

TABLE 8 - BASELINE SCENARIO RESULTS FROM THE SUTHERLAND PROJECT[139]

REVIEW GROUP	MEAN CHANGE		TOTAL AVERAGE COST ($)	MEDIAN COST ($)	COST QUARTILE ($)	
	DRUG COSTS ($)	HEALTH CARE COSTS ($)			LOWER	UPPER
Changes made (n=103)	-276.48	-218.90	-345.38	-229.83	-805.13	100.19
Changes recommended but not made (n=15)	-109.58	0	40.42	139.08	13.44	150.00
No changes recommended (n=23)	6.77	0	156.77	118.20	-9.60	155.04
TOTAL (n=141)	-212.52	-159.91	-222.43	-16.04	-543.99	150.00

Negative numbers denote savings. All values are annual costs or savings

Aside from the lack of an uncertainty analysis, the economic analysis undertaken in this study was comprehensive. The overt costs and consequences resulting from the medication reviews were accounted for, and the sensitivity of the economic model to key assumptions was thoroughly tested.

For example, an overt issue with the baseline scenario relates to the changes in drug costs. In the baseline scenario, the authors attribute all of the savings in all of the groups to the medication reviews, which is inconsistent with what actually occurred. In one quarter of cases, there were either no recommendations made in the reviews, or the recommendations were not implemented by the GP. Hence, it seems unlikely that the drug cost savings in these groups can be attributed solely to the medication review. Whilst some of the savings may have resulted from the reviews, a more appropriate analysis would have been to only consider the changes in drug costs when a recommendation was implemented by the GP. This was assessed in the sensitivity analysis, where changing medication costs to zero in these two groups reduced the average saving resulting from the medication reviews by only $10.56 (to $211.87).

The sensitivity analysis provides some valuable insight into factors that may influence the cost-effectiveness of the reviews. The factors to which the model was most sensitive were changes in medication costs and reimbursement levels. The authors focussed primarily on investigating the effect of reducing the reimbursement for pharmacists and GPs in the analysis. Only one scenario involved increasing the cost of the review service; increasing the cost of the reviews to $200 reduced the cost-effectiveness of the service by 22% (however, costs were still completely offset). With regards to drug

costs, using the lower and upper quartile of drug cost changes (as shown in Table 8) resulted in the reviews essentially breaking even or more than doubling the potential savings respectively. Changes to the health care resource utilisation costs resulted in less pronounced impact on cost-effectiveness. Based on these findings, it is apparent that significant savings from reduced drug costs are largely responsible for offsetting the additional costs incurred by providing HMRs.

1.3.1.3 St. George Canterbury Medico/ Pharmacy Project (Bennett *et al*. 2000)

The effect of HMRs on reducing drug costs was further explored in the St. George Canterbury Medico/ Pharmacy Project.[142] This longitudinal study was conducted in two general practice divisions in New South Wales and aimed to develop a sustainable, cost-effective medication review model. Two models of medication review were trialled as follows:

- Model 1: GP initiated, pharmacist-conducted mediation review
- Model 2: initial clinical audit conducted by GP who then initiated a pharmacist-conducted mediation review

Model 1 is that which was eventually implemented in the HMR model (Figure 2). The clinical audit in the second model involved the GP assessing the patient's management against a recognised practice standard and implementing changes for the patient's care to meet the standard where appropriate. The rationale for this additional stage was to assist the GPs in identifying the areas where medication review would benefit the patient's outcomes.

The outcome measures were cost of medications and QOL (assessed using the Dartmouth COOP Functional Health Assessment charts[137]). These were assessed at baseline and three months after the medication review for patients in Model One, and baseline, post-clinical audit and three months after medication review for patients in Model Two. The drug cost data were used to perform a cost analysis; there was no consideration of the cost of providing the reviews. No differentiation was made between drugs subsidised by the Pharmaceutical Benefits Scheme (PBS) and private items, so the perspective of the cost analysis is unclear.

Three hundred and eighty two patients were recruited for the study, and were randomised according to GP practice to receive either Model One or Model Two reviews. At follow-up, the mean decrease in monthly cost of medication in the Model One arm was $27.51 ($P$<0.005), compared to $10.77 ($P$<0.005) in the Model Two arm. The savings resulted from reductions in most drug classes in both cost and prevalence of patients taking (Table 9). Only anticoagulant drugs showed an increase in cost. Notably, when extrapolated to 12 months duration, the saving was $330.12 in the Model One arm, which is substantially more than the $212.52 reported in the Sutherland project (although this was performed three years earlier). The results regarding QOL were less positive. In both arms, there was a reduction in QOL scores at follow-up, with no differences between the two models.

TABLE 9 - DRUG COST SAVINGS THAT OCCURRED IN THE ST. GEORGE CANTERBURY STUDY (BOTH STUDY ARMS COMBINED) [142]

DRUG CLASS	PERCENTAGE OF PATIENTS TAKING			COST ($)		
	BASELINE	FOLLOW-UP	% CHANGE	BASELINE	FOLLOW-UP	% CHANGE
Cardiac	93.9	93.6	-0.3	27 642	25 879	-6.4
Analgesic	65.5	59.1	-9.8	3 204	3 002	-6.3
Coagulants/anti-coagulant	58.3	54.1	-7.2	1 192	1 792	50.3
Gastrointestinal	56.6	51.1	-9.7	9 170	8 429	-8.1
Endocrine	55.5	55.7	0.4	10 447	10 053	-3.8
Musculoskeletal	43.6	43.9	0.7	2 281	2 048	-10.2
Psychotropic	43.4	38.7	-10.8	2 961	2 640	-10.8
Vitamin	39.5	32.9	-16.7	1 389	928	-33.2
Respiratory	37.0	30.4	-17.8	7 224	6 087	-15.7
Eye	20.7	16.3	-21.3	1 640	1 339	-18.4
Dermatological	16.0	9.9	-38.1	715	392	-45.2
Neurological	13.5	13.3	-1.5	997	742	-25.6
Genitourinary	8.0	6.1	-23.8	493	336	-31.8
Anti-microbial	7.7	4.4	-42.9	1 088	732	-32.7
Immunomodulator	6.6	6.1	-7.6	2 367	1 732	-26.8
Anti-allergy	5.5	3.6	-34.5	276	99	-64.1
Ear, nose & throat	0.8	0.6	-25	n/a	n/a	n/a

This study compared two models of medication review rather than medication review to usual care; hence it did not demonstrate that the total drug cost savings resulted solely from the pharmacists' medication reviews. As with the Sutherland project and

the study by Greenhill, it is possible that other factors may have accounted for some of the drug cost savings. Furthermore, the duration of follow-up in this study was short (3 months). This raises questions regarding the validity of extrapolating the monthly drug cost savings to 12 months, as the changes may not have been sustained. In some patients it may have been necessary to revert to original drugs or undo dose reductions or drug cessations if the changes that were implemented were not effective or tolerated.

1.3.1.4 Quality Use of Medicines in the Community Implementation Trial (Gilbert *et al*. 2000)

To date, the largest Australian study of medication reviews is the Quality Use of Medicines in the Community Implementation Trial (QUMCIT).[86, 126] This was an uncontrolled observational cohort study where 1020 medication reviews were performed by 64 pharmacists during a 9-month period between 1999 and 2000. QUMCIT aimed to investigate the sustainability, acceptability and cost-effectiveness of medication reviews undertaken in six general practice divisions in South Australia.

The acceptability of the program was assessed using a combination of qualitative and quantitative methods. A component of the quantitative assessment investigated the number and rate of resolution of the DRPs identified in the medication reviews. Within three months of each medication review, any actions taken to address the DRPs identified were recorded from the patient's notes. No clinical outcomes were directly measured. The only patient data directly measured involved a survey of 24 patients, but this did not include a QOL measurement.

Despite the lack of empirical data collected in the study, the cost analysis performed in QUMCIT is the most comprehensive economic evaluation undertaken for HMRs to date. A description of both costs and benefits was provided, and the authors clearly stated the perspective of the analysis. As with the Sutherland project, the remuneration for pharmacists and GPs was substantially less than current HMR levels. Pharmacists were paid $100 per review, and GPs $50. In addition to the direct cost of each review, the study also considered the costs associated with implementing the program and providing the service to isolated rural localities. This is the only Australian study to

consider these substantial costs, which were estimated to amount to $495 000 over the first three years of the program in South Australia alone.[86]

As no empirical patient-level cost data was collected, the healthcare resource savings resulting from the medication reviews were estimated by experts. Initially, a random sample of 149 medication reviews was assessed by two research pharmacists. They predicted the potential reductions in costs resulting from GP visits, specialist visits, visits to other health professionals and hospitalisation in the 12 months following the review. The panel also estimated incremental costs incurred as a result of the reviews due to laboratory tests, administration aids and drug regimen changes. Importantly, the drug cost measurement contrasts with the three studies discussed previously which costed drugs at baseline and at follow-up. To strengthen the robustness of these estimates, the assessment was repeated by a group of four experts (two pharmacists and two GPs) on a sample of 30 DRPs from the 149 assessed reviews using the same methodology used by March *et al*.[44] A sensitivity analysis was then employed to explore the impact of changes to net savings and costs resulting from the service. No uncertainty analysis was performed.

As with the Sutherland project, the findings of QUMCIT indicated that the savings generated by the medication reviews would completely offset the cost of providing them. The estimated savings and incremental costs are shown in Table 10. It was estimated that the average savings per patient was $120 after accounting for the costs of the review and additional health services. Furthermore, these savings were sufficient to offset the infrastructure costs required to implement the program, which were not considered in the Sutherland project. The sensitivity analysis indicated that the program would offset total costs so long as the pharmacist and GP remuneration levels remained less than approximately $207 per review, or the average net savings were not less than approximately $212 per review.

TABLE 10 - HEALTH RESOURCE SAVINGS (TOP) AND INCREMENTAL COSTS INCURRED (BOTTOM) IN QUMCIT

HEALTH RESOURCE SAVINGS		
HEALTH RESOURCE	**COSTS ($)**	
	AVERAGE	**RANGE**
GP visits	-25.36	-22.22 to -28.49
Specialist visits	-6.89	-6.09 to -7.68
Visits to other health professionals	-1.79	-1.64 to -1.95
Hospitalisation	-280.59	-207.16 to -354.02
TOTAL COSTS AVOIDED	**-314.62**	**-237.11 to -392.07**

INCREMENTAL COSTS INCURRED	
HEALTH RESOURCE	**AVERAGE COSTS ($)**
GP Visits	11.45
Lab tests	8.59
Other tests	3.21
Specialist referrals	13.60
Education programs	0.00
Administration aids	1.20
Medication changes	2.29
Other	4.71
INCREMENTAL COSTS INCURRED	**45.06**

Negative numbers denote savings. All values are annual costs or savings

Notably, the source of the savings in QUMCIT was very different to the Sutherland project. The average predicted savings in health resources was $315 per patient - substantially more than the estimate of $159.91 in the Sutherland project. This may have resulted from differences in the composition of the expert panels employed to predict the outcomes of the HMRs, as substantial variability has been found between different types of experts when rating pharmacists' interventions.[143] Furthermore, QUMCIT did not demonstrate that any savings resulted from reduced drug costs - in fact, the results indicated that drug costs *increased* as a result of the reviews. This result must be interpreted in consideration that this was predicted change, as opposed to the previous three studies that actually measured drug costs. Therefore, it may be argued that the results of QUMCIT regarding drug cost changes are less robust than the other studies. However, despite these contrary findings, the only randomised control study that investigated the economic outcomes of HMRs found no change in drug costs occurring as a result of HMRs, discussed below.

1.3.1.5 Domiciliary Medication Review Project (Sorensen *et al*. 2000)

Of the five QUM evaluation program projects, only the Domiciliary Medication Review Project was of a randomised control design.[66, 144] This study was conducted in Queensland, New South Wales and Western Australia, whereby 400 patients were randomised according to their GP to receive either a HMR or usual care. The effectiveness of the HMRs was assessed in terms of:

- quality of life (using SF-36);
- participant satisfaction;
- clinical outcomes (number of ADEs, GP visits and hospital services, and severity of illness); and
- costs (of the intervention, medications and health services).

Patient data was collected over a six month period between 1999 and 2000.

The reimbursement model for pharmacists and GPs in this study was complex in comparison to the previous three studies. Pharmacists were paid $95 for the HMR and between $20 and $50 for a follow-up phone call with the patient's GP. GPs were reimbursed $38.55 for generating the HMR referral, between $20 and $80 for a follow-up phone call with the pharmacist and $120 for developing a medication management plan following the HMR. The average cost of a HMR per patient was $275.[viii]

At follow-up, there were no significant differences identified between the HMR and control patients in any of the outcomes measured, including drug costs, health resource utilisation costs and quality of life. However, non-significant trends were identified in reduced severity of illness, GP-reported ADEs and medical service costs per patient. Consequently, the net cost saving per HMR patient was a non-significant $54 relative to control. Figure 3 illustrates the cumulative cost per person for medication and medical costs in this study. Interestingly, there was no trend towards reduced medication costs, which is contrary to the findings of the St George Canterbury and Sutherland studies, but consistent with the estimates made in QUMCIT.

[viii] This is less than the figure calculated by summing the minimum reimbursement values for pharmacists and GPs ($293.55). Presumably a number of GP or pharmacist participants failed to claim for their involvement in the study

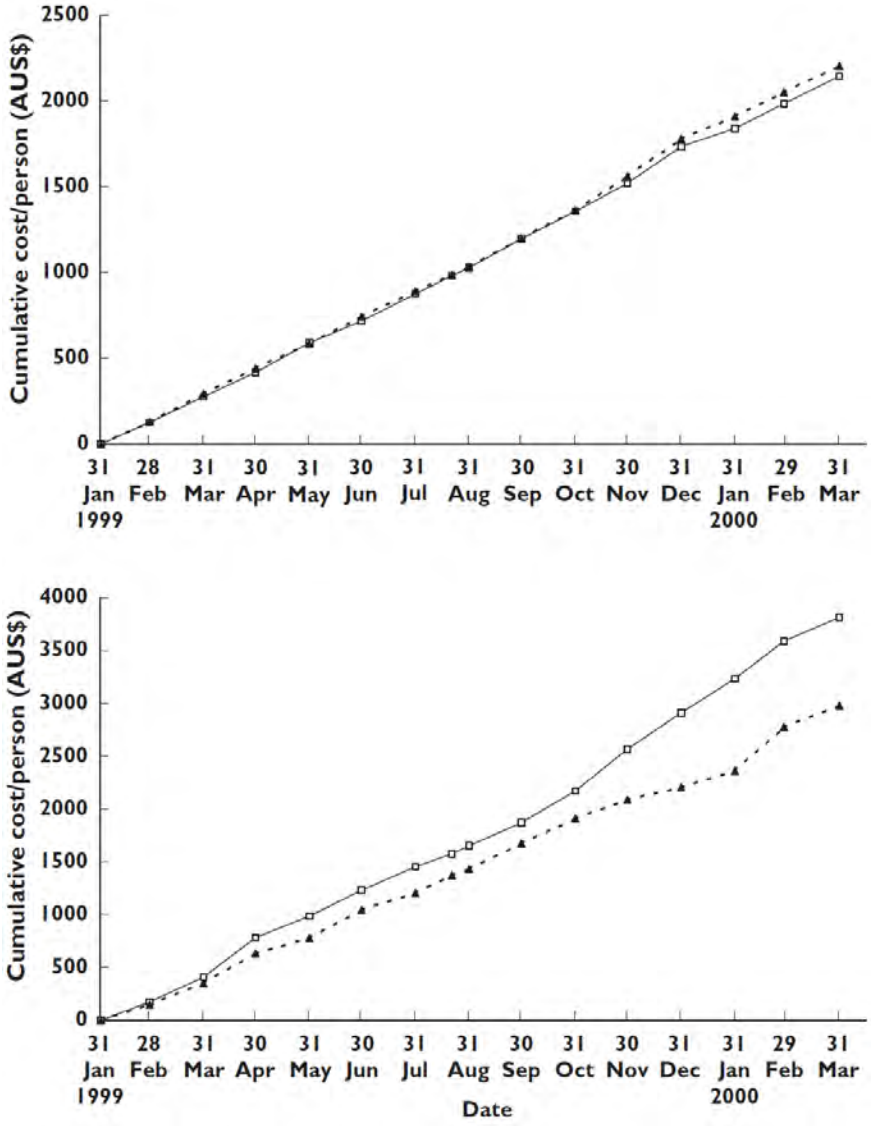

FIGURE 3 - CUMULATIVE COSTS PER PERSON (AU$) FOR PATIENTS ENROLLED IN THE DOMICILIARY MEDICATION REVIEW PROJECT IN TERMS OF MEDICATION COSTS (TOP) AND MEDICAL COSTS (BOTTOM). DASHED LINE INDICATES INTERVENTION PATIENTS; SOLID LINE DENOTES CONTROL PATIENTS. REPRODUCED FROM SORENSEN ET AL.[66]

The design and reportage of the Domiciliary Medication Review Project has been described as exemplary and a model that should be emulated in future studies of medication review.[114] A major strength to this trial is that each of these parameters was directly measured from the perspective of the Australian government. For example, drugs were costed by accessing patient's PBS drug costs. Similarly, health resources

were costed using Medicare Benefits Schedule (MBS) claims data. Whilst the study was of an excellent design, the economic analysis was somewhat limited by the lack of reporting of uncertainty and sensitivity analyses, especially in regards to the cost of providing the HMRs. Nonetheless, this study provides the highest level of evidence of the clinical and economic outcomes of HMRs to date.

A summary of the design and outcomes of the five MMR-related QUM Evaluation Program projects is presented in Table 11.

TABLE 11 - DESIGN AND RESULTS OF MMR-RELATED QUM EVALUATION PROGRAM PROJECTS

STUDY	DESIGN & PARTICIPANTS	ECONOMIC ANALYSIS & OUTCOME MEASURES	RESULTS	COMMENTS
Greenhill (1996)[136]	Uncontrolled observational cohort study; 62 patients received medication review at GP surgery by a single pharmacist.	CCA; cost and number of drugs, GP visits, compliance, drug knowledge and QOL.	Intervention resulted in average annual drug cost saving of $83.58 per patient; no differences in number of GP visits, drugs taken, dose times or daily doses.	Intervention not clearly described. Limited documentation of many measured outcomes. Cost of intervention not considered.
Sutherland Project (1997 - 1999)[138-140]	Uncontrolled observational cohort study; 275 patients received HMR.	CA; cost and number of drugs, health service utilisation costs.	Intervention resulted in reduced drug and health service costs- estimated average annual saving of $372.43 per patient. Cost of HMR ($150) totally offset.	Health service utilisation costs estimated by clinical panel.
St. George Canterbury Medico/ Pharmacy Project (2000)[142]	Uncontrolled observational cohort study; 382 patients received one of two models of medication review; model I (HMR only) and model II (clinical audit by GP followed by HMR).	CCA; drug cost and QOL.	Drug costs reduced in both models: monthly savings of $27.51 ($P$<0.005) and $10.77 ($P$<0.005) in Model I and II respectively. No difference in QOL.	Short (3 month) follow-up. Cost of intervention not considered.
Quality Use of Medicines in the Community Implementation Trial (2000)[86, 126]	Uncontrolled observational cohort study; 1020 patients received HMR.	CA; drug and health service utilisation costs.	Intervention estimated to result in reduced health service costs- estimated average annual saving of $314.62 per patient. Slight increase in drug costs ($2.29 per patient). Cost of HMR ($150) totally offset.	Health service utilisation and drug costs estimated by clinical panel.
Domiciliary Medication Review Project (2000)[66, 144]	RCT; 177 patients received HMR; 223 patients usual care.	CEA; QOL, severity of illness, ADEs, health service utilisation and drug costs.	HMR cost $69 per ADE avoided; $65 per DUSOI-A unit gained. Average saving of $54 per intervention patient (NS). Slightly increased drug costs in intervention group (NS).	Substantial missing data available for intervention patients-62% of HMR reports and 60% of follow up visits analysed.

CA: cost analysis; CCA: cost-consequence analysis; RCT: randomised control trial; CEA: cost-effectiveness analysis; NS: non-significant

1.3.1.6 Discussion

Having reviewed the five studies that were pivotal in the implementation of the Australian HMR program, it is apparent that the clinical and economic outcomes of HMRs cannot be definitively characterised based upon the evidence the studies provide. The studies clearly demonstrated that HMRs were possible using a collaborative MMR model, but their results in terms of effectiveness of HMRs were much less consistent. Whilst each investigated the cost-effectiveness of HMRs, there was substantial variation in the type of cost-effectiveness analysis performed and the costs considered, and consequently there was large variability between their findings.

In terms of drug costs, three of the studies (Greenhill, the Sutherland Project and the St. George Canterbury Medico/ Pharmacy Project) concluded that HMRs reduce drug costs,[136, 139, 142] whereas the remaining two (QUMCIT and the Domiciliary Medication Review Project) reported negligible changes.[66, 86, 126, 144] There are two potential reasons for the discrepancies between the findings of these studies. The first involves the perspective taken for drug cost measurement. In the Sutherland Project, drugs were costed using a combination of the PBS dispensed price and the costs to patients for non-PBS items (it is unclear from the reports how drugs were costed by Greenhill and in the St. George Canterbury Medico/ Pharmacy Project). Conversely, in QUMCIT and Domiciliary Medication Review Project, only drug costs to the PBS were considered and not the costs to patients. It is possible that the major savings reported by Greenhill, the Sutherland Project and the St. George Canterbury Medico/ Pharmacy Projects involved savings to patients rather than the PBS. However, the St. George Canterbury Medico/ Pharmacy Project reported reduced costs across virtually all drug classes. As the level of PBS subsidy would have varied considerably between the drug classes, this explanation is unlikely to account for the entirety of the variability in the findings between the different studies.

A more plausible reason involves consideration of the relative frequencies of the DRPs identified in the studies. The lack of consistency between studies in the classification of DRPs makes comparisons between them difficult; however, several general observations can be made. In the Sutherland Project, less than 1.5% of the DRPs identified involved too-low doses or untreated indications. Greenhill and the St. George Canterbury Medico/ Pharmacy Project did not report on the type or frequency

of DRPs identified in the medication reviews in their studies, and it is possible that the number of DRPs identified involving untreated indications was also low. Approximately 25% of the DRPs identified in the QUMCIT involved the need for additional therapy or dose increases. The frequencies of these types of DRPs were not explicitly stated in the Domiciliary Medication Review Project, but they appear to be at least equal to the frequencies of DRPs likely to result in drug cessation or dose decreases. It may be therefore be argued that characterising the type of interventions made in HMRs (that is, the nature of the DRPs identified and the recommendations made to resolve or prevent them) is an important facet of any investigation into the effect of HMRs on drug costs.

Similarly, it is not possible to draw definitive conclusions about the effect of HMRs on the cost of health resources other than drugs based on the results of these five studies. Using expert opinion, both QUMCIT and the Sutherland Project predicted that HMRs would substantially reduce health resource costs, although the magnitude of these estimates varied two-fold. QUMCIT reported that nearly 90% of the predicted savings resulted from averted hospitalisations. No breakdown of the type of health resource utilisation savings was provided in the Sutherland Project (that is, GP visits, specialist visits, hospitalisation *et cetera*), so it is unknown where the savings were predicted to occur. In contrast to these predictions, the Domiciliary Medication Review Project (which used observational data instead of expert opinion) reported no differences between the HMR and control groups for the number of hospital admissions, number of non-admission hospital services, cumulative number of bed-days and number of GP visits. The trend towards reduced costs in these parameters in the HMR group noted in the study suggests that there is some reduction; however, it is unlikely that they are of the magnitude predicted in the QUMCIT and the Sutherland Project. Finally, the level of pharmacist training and mentoring varied considerably between the studies, which may have accounted for some of the differences in the studies' findings.

1.3.2 Recent Australian and international literature

In light of the somewhat confusing and contradictory findings of the five early QUM implementation studies, it is relevant at this point to review the more recent Australian and international literature involving MMRs undertaken in the primary care environment. Each of the studies discussed in the following section investigated

the clinical and/or economic outcomes of MMRs in a setting similar to that in which HMRs are undertaken. However, as the models of medication review used in many of these studies differed from the Australian HMR model, and there was likely to have been substantial variability in pharmacist training and clinical acumen, the findings of these studies cannot be directly extrapolated to HMRs.

1.3.2.1 Department of Veterans' Affairs Domiciliary Visit Evaluation (2000)

In 2000, the DVA commissioned an evaluation of its medication review program which had commenced in 1994.[145] In this study, 92 veterans who received medication reviews between 1997 and 1999 were matched by age and number of regular medications with 19 veterans who did not receive MMRs. The outcomes measured were health service (GP visits, MBS items and private hospital admissions) and medication usage in the 24 weeks before and after the MMR for the intervention group, and for the same time period in the control group. All outcomes were measured using data in the DVA database; no investigation was directly undertaken into the MMRs. Consequently, changes to drug therapy were estimated using dispensing data rather than being directly measured, and no QOL measurement was performed. Additionally, interpreting this study's findings is complicated by several factors. Firstly, the only documentation of the study is a brief report to the DVA rather than publication in peer-reviewed medical literature. Furthermore, there were significant differences in several baseline characteristics between the two groups, and the statistical analysis is presented incompletely and is difficult to interpret.

Despite these limitations, there were several noteworthy findings reported at follow-up. With regards to drugs, there was a trend for the number (but not the cost) of medications in the MMR group to have increased. A significantly greater number of veterans in the MMR group had drugs commenced or ceased after the intervention compared to the control group, whilst a greater number of control veterans had no changes in their drug regimen than MMR veterans. In contrast, a trend towards increased health service costs was noted in the control group compared to the intervention group. Whilst hospital admission data was collected (42 hospitalisations occurred in the MMR group and 11 in the control group), the reasons for admission were undocumented and consequently the authors did not analyse this data.

Furthermore, data regarding admissions to public hospitals were not available to the researchers, which may have accounted for a substantial portion of the total number of hospitalisations in the cohort.

In view of its equivocal findings and significant limitations, the authors concluded that larger, better designed trials would be required to definitively assess the outcomes of MMRs. At best, it seems reasonable to consider that this study provides evidence that MMRs result in changes to patients' drug regimens, without identifying the clinical or economic outcomes of these changes.

1.3.2.2 Zermansky *et al.* (2001)

Zermansky *et al.* conducted a randomised control trial of medication reviews undertaken for community dwelling patients in general practice.[146] In this study, 1188 patients aged 65 years or older were randomised to receive either a medication review by a pharmacist or usual care. However, despite the large numbers of patients involved in the trial, a significant limitation of this study is that all reviews were performed by a single pharmacist.

The primary outcome measure was the number of changes that had been made to repeat prescriptions 12 months after the intervention. Secondary outcome measures were changes in number and cost of all medications, frequency of dose, and effect on GP consultations, hospital outpatient attendances and acute hospitalisations; QOL was not measured. The economic analysis performed in this study was limited by the authors not undertaking a sensitivity or uncertainty analysis. Interestingly, Zermansky *et al.* collected data on health resource utilisation based on the hypothesis that the intervention would not *worsen* patient health; this was in contrast to the more frequently made assumption that medication reviews *improve* patient health - an assumption made in a later publication by the same author.[114]

At follow-up, the intervention group had had significantly more changes made to their medication regimen than the control group (mean number of changes per patient 2.2 versus 1.9; difference 0.3, 95% CI 0.06 to 0.57, P=0.02). Although medication costs rose in both groups, the rise in the intervention group was significantly less than the rise in the control group by £61 per year. No significant differences between the two

groups were identified with regard to GP consultations, hospital outpatient attendances or acute hospitalisations.

The medication reviews in this study were performed at the GP surgery, and the pharmacist was permitted to implement many minor changes without involving either a GP or practice nurse. Any major changes were discussed with a GP at the time of the review. As a result, the medication reviews were very brief, with an average of 20 minutes to conduct a review. Consequently, delivering the intervention was inexpensive in comparison to the Australian HMR model - each review was costed at only £7, calculated on the gross cost of the pharmacist's involvement (£21 per hour). This cost was totally offset by the drug-cost savings attributed to the medication reviews.

Zermansky *et al.* concluded that their model of medication review resulted in more changes to treatment than normal care and produced "*important cost savings, even after the cost of the intervention was deducted*".[146] However, the calculation of costs to deliver the medication reviews appears simplistic. The figure of £21 per hour only included costs such as:

- the cost of using a consultation room at the GP surgery (e.g. electricity, not using the room for GP consultations etc.); and
- the additional time required by the GPs and practice nurses to discuss the interventions and implement changes if required.

Furthermore, as the authors acknowledged, the involvement of only one pharmacist is a significant limitation to the study.

It is important to note that the model and setting of review in this study differed substantially from the Australian HMR model. Not only were the reviews performed at the GP surgery as opposed to the patients' home or site of choice, they were also undertaken without a referral by the patient's GP. The authors asserted that "*a clinical medication review undertaken by another health professional is only useful if it can be undertaken without having to routinely involve the GP. If the patient needs to be referred to the GP or the GP's permission or opinion has to be sought frequently, then the GP may as well undertake the review.*"[147] However, collaboration between pharmacist and GP is

an integral part of the HMR model. Given these limitations and differences between medication review models, conclusions regarding the outcomes of HMRs cannot be reliably made from the results of this study.

1.3.2.3 Krska *et al.* (2001)

Krska *et al.* conducted a randomised controlled trial investigating the effect of MMRs undertaken for patients in the Grampian region of Scotland.[47, 148] Patients were aged over 65 with at least two chronic diseases and taking at least four "repeat" (chronic) medications. The outcome measures in this study were number of DRPs, medication costs, use of health and social services (such as district nurses) and health-related quality of life (using SF-36). Outcomes were measured at baseline and three months after the medication review. An unspecified number of pharmacists took part in this study, and little detail was provided regarding them other than they were "clinically-trained".

A comprehensive economic evaluation was not a component of this study's design. The only cost that was considered was medication costs - no costs were associated with the other health resources investigated (such as hospital clinic attendance, emergency hospitalisation or therapeutic monitoring). Neither was the cost of providing the medication reviews considered.

The reason for the lack of a comprehensive cost analysis in this study may be related to the study's design. Despite being a controlled trial, patients in both the control and intervention groups received medication reviews. Initially, a detailed medication profile for all patients was generated by pharmacists using the patient's medical notes. All patients were then interviewed at home, and DRPs were identified by the pharmacists. It is at this point that the actual intervention occurred. Patients in the control group were advised to consult their usual carers or health professionals when DRPs were identified in the medication review. For the intervention patients, following the patient interview, a care plan to address the identified DRPs was formulated and provided to the patient's GP. Hence, Krska *et al.* actually assessed the impact of providing care plans on the outcomes of medication reviews, rather than the impact of medication reviews versus usual care.

A total of 332 patients were involved in this study; 168 in the intervention group and 164 in the control group. At follow-up, significantly more DRPs had been resolved in the intervention group compared to the control group. However, there were no significant differences between the two groups with regards to average monthly medication costs or QOL. The analysis of health and social services utilisation was limited by small numbers of events in both intervention and control groups. A small increase in contact with health-care professionals and slightly fewer hospitalisations were identified in the intervention group. However, the authors reported that number of these events was too small to undertake any meaningful statistical analysis.

Krska *et al.*'s model of medication review shared more similarities with the Australian HMR model than that used by Zermansky *et al.* Although no referral was received from patients' GPs, Krska *et al.*'s model involved patients being interviewed in their own homes (rather than at their GP's surgery). Furthermore, the formulation of a care plan directly parallels the HMR model. However, as discussed previously, the intervention assessed by Krska *et al.* was the effect of a care plan rather than a medication review. As both groups included a medication review, it is likely that many of the benefits resulting from the medication reviews would have occurred in both patient groups. Only the proportion of DRPs requiring direct GP involvement to resolve would have been detected by the study, and so the "value" of medication reviews in this study is likely to be substantially understated.

Despite the small number of hospitalisations (77), a sub-analysis of this study was published which provides some insight into the use of hospitalisation as an outcome measure in studies of medication reviews.[148] In this analysis, the types of hospital admissions that occurred were described and the proportion of these admissions that could have been influenced by a pharmacist's intervention was assessed via expert opinion. The details of each admission were reviewed in a multi-stage process by a consultant in elderly care and a GP who determined whether or not DRPs contributed to the admission. Two pharmacists then judged whether or not the admissions resulting from DRPs were potentially preventable by pharmacist intervention.

In this analysis, only 17 of the 77 admissions (22%) were considered by the assessors to be related to DRPs. Of these 17 cases, 10 (13% of all admissions) were classified as being at least partially preventable by pharmacist intervention. Krska *et al.* concluded

from these results that total number of hospital admissions is not an appropriate outcome measure for evaluating pharmacist intervention. They asserted that a more appropriate outcome measure is either preventable admissions or medication-related admissions. The authors acknowledged that using this measure is a time-consuming process and requires a substantial amount of information about each admission be available. Consequently, few studies have used preventable or medication-related admissions as an outcome measure.

1.3.2.4 Naunton (2003)

One of the few studies of medication review that reported on the type of hospital admission was a small RCT conducted in Tasmania, Australia, by Naunton and Peterson.[149] In this study, patients aged 60 years and older who fulfilled certain high-risk criteria were randomised to receive either a medication review from a single study pharmacist five days post-hospital discharge (57 patients) or usual care (64 patients). The review model was not directly comparable to a HMR as the patient's GP did not refer the intervention patients for the review, although the pharmacist could access the patient's medical history from hospital records.

Follow-up data was collected 90 days after discharge. The primary outcomes measured were the number of unplanned readmissions (total and drug-related), total days of readmission and out-of-hospital deaths. Secondary outcomes involved a number of measures including compliance and number of DRPs. Although no costs or quality of life data were collected, this trial is worthy of discussion as it provides some insight into issues involved in assessing the outcomes of HMRs on hospitalisation.

At follow-up, there was a significantly lower proportion of patients in the intervention group with unplanned readmissions to hospital for any reason compared to the control group (P=0.05). Additionally, the duration of readmission showed a trend towards reduction in the intervention group (P=0.06). As with the study by Krska *et al.,* the number of drug-related readmissions in both groups was minimal within 90 days (3 intervention patients versus 2 control patients).

1.3.2.5 Seniors Medication Assessment Research Trial (2003)

A much larger study that used medication-related hospital admissions as an outcome measure was the Seniors Medication Assessment Research Trial (SMART).[64, 150] This cluster RCT conducted in Ontario, Canada, investigated the effect of "structured medical assessments" (medication reviews) conducted by pharmacists for community-dwelling patients aged 65 years and older who were taking five or more medications daily.

The primary outcome measure for the study was a reduction in the daily units of medications taken, which was chosen as a surrogate marker for optimised drug therapy. Secondary outcomes were the cost of medications, health service use (including medication-related hospital admissions), health-related costs and quality of life (assessed using SF-36). Outcomes were measured at baseline and five months after the intervention. A cost-consequence analysis was undertaken in the study using:

- medications;
- medication-related hospital stays;
- GP visits;
- laboratory investigations;
- surgical procedures;
- emergency/urgent care visits/ambulance use;
- hospital admissions (drug-related and otherwise);
- other health services utilised; and
- pharmacist time to perform the medication reviews.

The model of medication review used in SMART shared many similarities with the Australian HMR model. Participating pharmacists were all "expanded role pharmacists"-pharmacists who had received additional training regarding patient-centred counselling to detect and resolve DRPs. Each review involved the pharmacist interviewing the patient (albeit at their GP's surgery), and pharmacists had access to patient medical records. Following the interview, the pharmacist prepared a list of the patient's medications and any DRPs detected, which was discussed with the GP who

then implemented any relevant changes. Four hundred and thirty one patients received the intervention, compared to 458 patients who received usual care.

The GPs implemented a majority of the recommendations made in the medication reviews (approximately 57% of recommendations were at least partially implemented). However, no significant differences between the two groups with regards to any of the outcomes measured were detected at the 5-month follow-up, as shown in Table 12. Neither was there any significant difference found in quality of life. Interestingly, the only measure that showed a trend towards significance was medication-related hospital stays, although the numbers of these events was very small. Despite collecting a substantial amount of cost data, no comment was made by the authors regarding the cost-effectiveness of the intervention.

TABLE 12 - MEAN HEALTH RESOURCE UTILISATION AND COSTS FOR INTERVENTION AND CONTROL PATIENTS IN SMART TRIAL. MODIFIED FROM [64]

HEALTH CARE RESOURCE AND COST	INTERVENTION		CONTROL		*P*- VALUE
	NUMBER*	COST (CA$)	NUMBER*	COST (CA$)	
Daily medications	12.4	5.01 /day	12.2	4.82 /day	0.50
Physician visits	5.2 (0.3)	203.96 (11.13)	5.0 (0.3)	198.3 (10.44)	0.65
Clinic visits	0.3 (0.15)	18.81 (8.05)	0.3 (0.60)	20.94 (5.04)	0.40
Laboratory tests/ imaging procedures	8.7 (0.6)	249.34 (20.82)	8.6 (0.1)	243.1 (17.21)	0.60
Surgical procedures	0.5 (0.2)	221.18 (68.3)	0.7 (0.3)	253.66 (88.09)	0.32
Emergency/ urgent care visits and ambulance use	0.20 (0.03)	36.28 (5.55)	0.23 (0.03)	41.88 (6.86)	0.28
All admissions to hospital	0.14 (0.02)	753.74 (183.12)	0.11 (0.02)	594.89 (135.19)	0.77
Drug-related hospital stays	0.04 (0.01)	142.51 (42.82)	0.04 (0.01)	248.54 (82.52)	0.08
Other health care services/ visits to health professionals	7.8 (1.2)	288.3 (40.02)	7.8 (1.3)	293 (55.25)	0.47
Time spent with pharmacist, minutes	72.8 (2.9)	75.06 (2.95)	0.0 (0.0)	0 (0)	-
Total costs					
all hospital stays included	1894.10 (200.66)		1644.69 (220.84)		0.83
only drug-related hospital stays included	1281.27 (101.42)		1299.37 (154.74)		0.45

Bracketed values indicate standard error; * unless stated otherwise

The interpretation of these results by the trial's authors was somewhat optimistic. Despite the lack of any clinically significant outcomes, the authors concluded that the high rate of acceptance of the pharmacists' recommendations was evidence that intervention improved the quality of pharmacotherapy. In an invited commentary, Majumdar and Soumerai published a more objective interpretation of the trial and its results.[151] Aside from the potential that the intervention was ineffective, they suggested another reason for the lack of any clinically significant outcomes.

Majumdar and Soumerai postulated that the primary outcome measurement in the study was inappropriate according to the prevalence of the different DRP types identified by the pharmacists. More DRPs relating to inadequate therapy than unnecessary therapy were identified, hence more recommendations were made to commence new medications compared to ceasing current medications. Majumdar and Soumerai therefore asserted that the outcome of reducing the number of medicines taken was misdirected. As numerous other studies have identified that DRPs involving the under-treatment of chronic disease are at least as common as over-prescribing, such criticism is probably justified.[68, 71, 152, 153]

Another explanation of the insignificant results was proposed by Dolovich *et al.*[154] They investigated the anticipated time to clinical impact of the recommendations made by the pharmacists. They identified that only 15% of the recommendations made by the pharmacists were likely to have moderate or marked impact on patient symptoms or health outcomes during the five-month follow-up period. However, they did not estimate how long the period of follow-up should be in future studies for a greater proportion of benefits to be realised.

1.3.2.6 Graffen *et al.* (2004)

Graffen *et al.* published the only Australian randomised controlled trial since the implementation of the HMR program that assessed the outcomes of HMRs.[120] In this study, 402 patients in rural New South Wales who fulfilled criteria similar to those used to identify patients for HMR were randomised to receive either a HMR or usual care. The outcomes measured were quality of life (measured using SF-36) and hospitalisation (number and cause) six months after the HMR. As with the study by Zermansky *et al.*,[146] a significant limitation of this study is that all reviews were

performed a single pharmacist. Cost data was not collected, and an economic analysis was not undertaken in this study.

At follow-up, 91 patients had been hospitalised; however, only two patients' admissions were medication-related, which is consistent with the findings of Krska *et al.*[47] There was no significant difference in hospitalisation rates between intervention and control groups. Similarly, there were no significant differences in overall QOL scores. The intervention patients recorded significantly higher scores in the domains of vitality and mental health post-intervention compared to their pre-intervention scores, but the magnitude of these changes was not provided.

In discussing the improvements in vitality and mental health, Graffen *et al.* were cautious in attributing the benefits solely to HMR. They suggested that the benefits may have occurred as a result of increased interaction with GPs or other changes to the patients' circumstances (such as pet ownership) that were not measured in the study. Regardless, the study concluded that HMR was unlikely to worsen QOL or increase hospitalisations.

1.3.2.7 Evaluation of the HMR program (Pharmacy component) (2005)

In 2005, the Pharmacy Guild of Australia and the Australian Government Department of Health and Ageing commissioned an evaluation of the pharmacy and GP components of the HMR program to inform government whether funding should be continued into the Fourth Community Pharmacy Agreement.[15] As of December 2011, the report detailing the GP component assessment has still not been released for public viewing, and no peer-reviewed papers detailing the pharmacy component of the research have been published. However, it is important to review this report as its findings resulted in continued funding for the HMR program in the fourth Community Pharmacy Agreement.

A primary aim of the pharmacy component project was to undertake an economic evaluation of HMRs from three perspectives-consumers, pharmacists and the health system. This study used several data sources to evaluate the program:

- a survey of 1702 pharmacists, in which pharmacists estimated the numbers and clinical outcomes of the HMRs they had performed;
- a retrospective survey of 50 consumers who had participated in HMRs in the previous three to twelve months;
- seven case studies involving consumers, the participating pharmacists and the referring GPs; and
- the results from the economic analyses in the St. George Medico/ Pharmacy Project and QUMCIT.

In this study, clinical outcomes resulting from HMRs were assessed primarily using the results of the consumer and pharmacist surveys. Patients who had received HMRs were asked whether they had experienced significant health problems related to their medications before and after the HMR, and were also administered the EuroQol questionnaire (EQ-5D) to quantify utility scores. However, a significant limitation of this study's QOL measurement is that the questionnaire was administered twice at the same time. Respondents were initially asked to answer the questionnaire according to how they recalled feeling before the HMR, then the questionnaire was repeated and the respondent answered according to how they felt presently. The questionnaire was administered at the end of the interview. It is therefore possible that the responses were more reflective of their satisfaction with HMRs rather than their QOL, as most patients were highly complimentary of HMRs.

The consumer survey reported a gain in the mean QOL utility score of 0.119, and the greatest improvements occurred in the domains of anxiety/depression and pain. When considered in conjunction with the data from St. George Medico/Pharmacy Project and QUMCIT, the evaluation concluded that HMRs are highly cost-effective in terms of cost per QALY gained and delivering net future benefits. The study reported that the HMR program completely offset costs, saving $4.5 million Australia-wide in 2004, whilst resulting in gain of 1435 QALYs.

However, these conclusions must be viewed in consideration of the limitations into the data sources highlighted previously, and are of dubious validity. The study used drug cost savings data from the St. George Medico/ Pharmacy Project and savings to the health system from QUMCIT, the two trials reporting the greatest savings in these parameters, respectively. Furthermore, an incorrect figure from QUMCIT was used to

value the health systems savings - the report used a figure of $120 saved per patient per annum, which actually included the cost of the HMR (the correct figure was $314.62, as shown in Table 10). As the report also costed HMRs using data provided by the pharmacists surveyed, the cost of the HMR was actually accounted for twice, so the savings to the health system (and thus the cost-effectiveness of the HMR program) should have been much greater! It may therefore be argued that the limitations and errors in this study invalidate its findings, and the estimate generated of the cost-effectiveness of the HMR program cannot be considered to be robust whatsoever.

1.3.2.8 Home-based Medication Review study (2005)

The home-based medication review trial (HOMER) investigated whether medication reviews conducted by pharmacists for older UK patients could decrease hospital readmissions.[25, 26, 155-157] HOMER was of a randomised control design whereby patients aged 80 years or older who had been admitted to hospital as an emergency were stratified to receive either two post-discharge medication reviews by a pharmacist or usual care. Reviews were performed within two and eight weeks of discharge. The primary outcome measure for the study was total number of emergency hospitalisations at six months; however, information relating to the cause of hospitalisation was not collected. Secondary outcomes included deaths, admissions to residential care homes, and self-assessed quality of life (assessed using the EQ-5D).

The economic analysis undertaken for the HOMER study is one of the most comprehensive evaluations of medication reviews published to date. Data regarding intervention costs (including pharmacist training, participation and administration), costs due to emergency hospitalisation, items prescribed and primary care costs were either collected or estimated for the economic analysis. Furthermore, an extensive sensitivity analysis was undertaken, and uncertainty was appropriately estimated using a nonparametric bootstrapping approach (described in Section 2.4.4).

Despite there being no accrediting body equivalent to the AACP or SHPA in the UK, the pharmacists involved in HOMER appear to have received similar training in medication review as Australian accredited pharmacists.[155] Twenty two pharmacists participated in the study. All held postgraduate qualifications in pharmacy practice or "recent continuing professional development in therapeutics". Additionally,

pharmacists participated in a two-day training course that focussed on ADRs, prescribing in the elderly, improving concordance and communication skills.

HOMER was a large randomised control trial where 429 patients received medication reviews compared to 426 control patients. However, the study did not find that medication reviews reduced hospital readmission; in fact, the rate of hospitalisation in the intervention group was 30% higher than that of the control group ($P<0.05$). Furthermore, there were no significant differences in any of the secondary outcome measures except for visual-analogue scale QOL scores, which were higher in the control group ($P<0.05$). In contrast, a non-significant difference in QOL in favour of the intervention group was identified in the EQ-5D descriptive system and years of life gained.

Based on the differences between the two groups in QOL and years of life gained, a cost-utility evaluation was undertaken from the perspective of the UK's National Health Service.[25] In the scenarios tested in the sensitivity analysis, only one indicated that the medication review model was cost-effective at a threshold of £30 000 per QALY gained (Table 13). The uncertainty analysis indicated that there was only a 25% probability that the intervention was cost-effective at this threshold in the baseline scenario.

TABLE 13 - RESULTS OF SCENARIO ANALYSES FROM THE HOMER TRIAL. MODIFIED FROM [25]

SCENARIO	MEAN DIFFERENCE IN UTILITY (QOL)	COST PER QALY GAINED (ICER, £)
Baseline	0.0075	54 454
Hospital stay cost model I	0.0075	77 875
Hospital stay cost model II	0.0075	60 118
Baseline with community costs considered	0.0075	50 879
Baseline with community and primary care costs considered	0.0075	61 634
Intervention cost only	0.0075	17 070
Baseline minus ambulance costs	0.0075	51 044

Despite the apparent robustness of the design of the HOMER study, its results and interpretation have been criticised by several authors (including pharmacists and physicians) for various reasons,[158-163] including:

- a greater proportion of patients in the intervention group compared to control were diagnosed with cancer or dementia (diagnoses which commonly require hospitalisation);[161, 162]
- a medical history was not available to the reviewing pharmacists, which may have limited the pharmacists' ability to gauge the appropriateness of each medication;[164]
- the patients' medication regimens may have been optimised during their initial hospitalisation, limiting the opportunity for the pharmacists to further improve prescribing;[165] and
- the reason for hospital readmission, and whether or not they were preventable, was not reported, a limitation present in the work by Krska *et al.* discussed previously.[148] In addition, a majority of admissions in the intervention group occurred in a very small number of patients[ix], which may have skewed the results significantly.

Perhaps the most insightful comment on the HOMER study was written by Mohammed,[166] who asserted that studies of medication review should investigate the cause of the outcomes, rather than simply the outcome itself. HOMER did not assess the nature of the interventions the pharmacists undertook, nor whether the recommendations the pharmacists made were enacted upon by the patients' GPs. As discussed previously, the cost-effectiveness of medication reviews seems to be related to the types of DRPs identified - and by not investigating the DRPs then cause of the outcomes is largely unknown.

A further consideration regarding this study is that, despite the similarities between it and Australia's HMR model, there are several notable differences. Primarily, the

[ix] Two patients in the intervention group were hospitalised 11 times, accounting for 20% of the total number of hospitalisations in this group. A further 15 hospitalisations (27%) occurred in five of the intervention patients. Hence, almost half of the hospitalisations occurred in less than 2% of the intervention patients

medication review in HOMER was not requested by the patient's usual GP, whereas an Australian HMR is initiated via a GP's referral. Holland *et al.* commented in an editorial that the most successful medication review interventions seem to involve close collaboration with GPs.[167] Furthermore, the patients reviewed in HOMER were all very old and recently discharged from hospital - whereas any home-dwelling Australian is eligible for a HMR. Hence, it is debatable whether the findings of HOMER translate to the Australian HMR model.

However, recent Australian data has raised some concern that the results of HOMER may be more applicable to Australia than initially thought. A RCT (total 120 patients) of post discharge medication reviews or usual care for Australian patients recently hospitalised with CHF was done by Barker *et al*.[168] Similarly to HOMER, the GP was not involved in referring the patients. There were no significant differences between the intervention and control groups with respect to mortality or number of hospitalisations. However, as with the HOMER study, there was a significant increase in both all-cause (RR=1.25, 95% CI 1.06-1.48, *P*=0.009) and CHF-related hospitalisation days (RR=2.34, 95% CI 1.80-3.05 *P*<0.001) in the medication review group. Again, the lack of certain aspects of the HMR model in this study make drawing similarities between it and HMRs questionable; however, it raises further concerns about the effectiveness of HMRs.

1.3.2.9 The POLYMED trial (2007)

To address the potential that a lack of GP-pharmacist interaction influenced the results of the HOMER study, the HOMER research group conducted a second RCT where the pharmacist liaised closely with the GP and practice team.[169] This study involved a similar cohort as the HOMER study- all patients were at least 80 years of age, living at home, taking four or more medications and considered to be at risk of medication misadventure. The primary outcome measure was the total number of non-elective hospital admissions at 6 months, with secondary outcomes including number of deaths, care home admissions and quality of life (measured using EQ-5D). The POLYMED trial was substantially smaller than the HOMER study; 69 intervention patients received medication reviews by a single pharmacist, with 67 control patients. Other major differences between the two studies include that the patients in

POLYMED were not recruited at hospital discharge, unlike those in HOMER, and the economic analysis was limited to costing the intervention (£112 per patient).

Of the outcomes measured, the only difference between the intervention and control groups was a reduction in the mean number of prescribed medications in the intervention group (difference in means 0.87, *P*=0.03). There were no differences in the number of hospital admissions, care home admissions, deaths or quality of life. The authors interpreted their findings as demonstrating that medication review services should not be implemented for all older patients; instead, they should target at-risk populations to maximise the benefits of the service. This was an interesting conclusion given that the study cohort was recruited specifically because they were considered to be at very high risk of medication misadventure. The authors provided no further commentary as to what "high-risk" characteristics may be used to identify patients who would benefit from MMR.

1.3.2.10 Community Pharmacy Medicines Management Project (2007)

The Community Pharmacy Medicines Management Project (CPMMP or MEDMAN) was a large RCT conducted in the UK that investigated the effects of medication reviews on a different at-risk population.[23, 59, 170] This study investigated the effect of a pharmacist-led "medicines management service" (essentially a medication review with additional visits if necessary) in 980 patients with coronary heart disease, compared to 513 control patients. Patients were followed-up at 12 months in terms of the following outcomes:

- receiving UK National Service Framework recommended therapy for secondary prevention of CHD;
- a cumulative score summarising the "appropriateness of treatment";
- QOL (using SF-36 and EQ-5D);
- cost-effectiveness (from a cost-minimisation perspective);
- 5-year risk of cardiovascular death;
- patient satisfaction with their most recent pharmacy visit; and
- compliance with treatment.

The cost analysis in the study included the cost of the intervention (£118 per patient), costs of treatment (pharmaceuticals, GP and hospital visits) and patient costs.

At follow-up, significant differences between control and intervention groups were identified in only two parameters - both satisfaction scores and total costs were higher in the intervention group compared to control ($P<0.01$ and $P<0.0001$, respectively). Although there were minor savings in terms of the total cost to the NHS (excluding the intervention), these were more than offset by the cost of the intervention. Sensitivity analysis indicated that the cost of the intervention would have to be reduced by 35% (to £76) for the cost difference between intervention and control to become insignificant. As a result of this analysis, the authors concluded that the intervention was unlikely to be an efficient use of healthcare resources. An analysis of the DRPs reported by the pharmacists suggested that there was a large range of clinical issues not addressed by them, which may have accounted for the lack of benefit resulting from the intervention.[59]

1.3.2.11 Holland *et al.* (2007)

A meta-analysis investigated the effects of medication review on all-cause hospital admission and mortality in older patients.[24] The analysis indicated that pharmacist-led medication review had no effect on all-cause hospital admission (relative risk of 0.99, 95% CI 0.87 to 1.14, $P=0.91$) or mortality (relative risk of 0.96, 95% CI 0.82 to 1.13, $P=0.65$). The only finding of statistical significance was a reduction in the number of medications prescribed (weighted mean difference=-0.48, 95% CI -0.89 to -0.07). Despite not including any assessment of cost-effectiveness in the analysis, these findings lead the authors to question the value of medication reviews and suggest that funding for such programs would be better spent on proven cost-effective interventions that reduce hospital admissions and mortality.

1.3.2.12 Denneboom *et al.* (2007)

Denneboom *et al.* conducted a clustered, RCT of "treatment reviews" undertaken for Dutch patients aged ≥75 years who were taking more than five medications.[171, 172] No clear definition of "treatment review" was provided; however, reference was made to methods used in studies such as that by Zermansky *et al.* discussed previously.[146]

Rather than compare patients who received a treatment review to no review, Denneboom *et al.* compared two different models of review. In one arm, written feedback only was provided to each patient's GP. In the other arm, a medication management plan was formulated during a case conference between the pharmacist and GP that occurred following the review. Consequently, the effect of the intervention compared to usual care was not assessed; rather, the study addressed the viability of incorporating case conferences in medication reviews.

The economic analysis for the study considered two costs:

- drug costs, which were assessed 6 and 9 months after the treatment reviews; and
- involvement of the healthcare professionals, costed at €50/hr.

An expert panel assessed the clinical relevance of the recommendations made by the pharmacists but no cost estimates were attributed by this process. The economic analysis was further limited by less than 40% of participating GPs providing time (and consequently costing) records, and QOL was not measured.

Seven hundred and thirty eight patients received treatment reviews: 351 in the written feedback arm and 387 in the case conference arm. The expert panel analysis of the clinical relevance of the pharmacists' recommendations indicated that the majority were of some clinical relevance (1516 of 1569 recommendations were classified as *potentially* or *actually clinically relevant*). In both groups, a modest reduction in medication costs was identified at both follow-up points (average yearly savings of €7.79 per patient in the written feedback group and €12.24 per patient in the case conference group). There was no significant difference between the two groups with regards to net expenses resulting from the treatment reviews, and consequently the authors concluded that case conferences should be included in models of treatment reviews for older patients as they are more effective and no more expensive. However, as there was no group of patients who did not receive MMRs, no conclusions regarding the cost-effectiveness of the MMRs can be drawn.

1.3.2.13 Krähenbühl *et al.* (2008)

In an uncontrolled observational study, Krähenbühl *et al.*[58] investigated the cost of drug therapy as a screening criterion for patients who may benefit from medication review in Switzerland. Patients were included in the sample if their drug costs exceeded US$1440 in a six-month period. The intervention in this study was theoretical - medications reviews were performed for 125 patients using the patients' pharmacy records, and the DRPs and resolving recommendations were documented. However, there was no contact between the pharmacists and the patients or their GPs, and no actual changes were made to the patients' drug regimens. The pharmacists also identified and made recommendations to resolve "expense problems" (EPs), presumably issues relating to medication costs. Changes to the cost of the drug regimen were then estimated by assuming that all of the pharmacists' recommendations were implemented. No estimate of savings to the health system or quality of life was generated, nor was the cost of the intervention accounted for.

DRPs and EPs were identified in 119 (95%) of patients. Had the pharmacists' recommended changed been implemented, it was estimated that the mean daily drug cost would have decreased from US$10.71 to $9.50, with the greatest savings resulting from "therapeutic switches" as opposed to "generic substitutions" or DRP resolution. Whilst an overall saving was identified, this was not universal across every drug class. The drug classes with the greatest potential savings were proton pump inhibitors, anti-asthmatic drugs and non-steroidal anti-inflammatory drugs (NSAIDs), with analgesics accounting for the greatest increased costs.

Whilst there are several shortcomings to this study that limit the robustness of its findings, it is interesting that its results are somewhat contrary to those of the St. George Canterbury Medico/ Pharmacy Project.[142] In that study, savings were noted to occur in virtually every drug class. It is possible that these differences resulted from differences in the medication review models and the assumption that every recommended change would be implemented. However, in consideration of the findings of the other trials discussed in this review, it seems unlikely that the drug cost savings reported in the St. George Canterbury Medico/ Pharmacy Project are generally realised in medication reviews.

1.3.2.14 Altavela *et al.* (2008)

Further evidence of this is provided by Altavela *et al.* who conducted a well-designed, prospective, controlled study that investigated the effects of medication reviews for patients of two primary care practices in New York, USA.[173] A single pharmacist reviewed the medical notes of patients in both groups, but only the recommendations made to resolve the DRPs identified in the intervention group were made available to the patients' physicians. There were minimal inclusion criteria for the patients; most related to risk factors similar to those used to identify patients for HMRs. In contrast to HMRs, the intervention was delivered at the patients' GP practice. A formal medication review was performed only once; however, the pharmacist provided additional counselling and education after the review, presumably each time the patient presented to the practice.

There were 343 patients enrolled in this study: 127 patients in the intervention group and 216 in the control group. The groups were not ideally matched, as the intervention patients were slightly younger than the control group (median age 59 years compared to 68 years, $P<0.001$) and visited their GP less frequently in the year prior to enrolment ($P=0.03$). The primary outcome was medical costs per patient per year, and included costs resulting from hospitalisations, emergency department visits, radiology, laboratory tests, GP visits and specialist visits. Prescription drug costs were not available on a per-patient basis, and were only considered as group aggregates. Patients were followed up at 6 and 12 months post intervention. These data were used to undertake a simple cost analysis with no consideration regarding the cost of providing the medication review service. QOL was not assessed.

At follow-up, there were no significant differences between the two groups regarding any of the costs considered in the analysis, although a trend in reduced emergency department costs was identified ($P=0.054$). Furthermore, the intervention group's prescription claims cost increased by 17%, whilst the comparison group's cost decreased by 10%. This may have resulted from the types of DRPs that were addressed. The DRPs with the greatest proportion of resolution in the intervention group were classified as *medication non-adherence* (86% of these DRPs were addressed in the intervention group compared to 40% in the control group, $P<0.001$)

and *untreated indications* (73% versus 11%, *P*<0.001). The resolution of both of these types of DRP would most likely have resulted in an increased use of medication.

Based on these results, it appears unlikely that the service would have been cost-effective unless there was a significant improvement in QOL in the intervention group compared to control. It is possible that, had a longer follow-up occurred, the benefits resulting from improved adherence and reductions in untreated conditions may have resulted in health care savings. However, the duration of follow-up would have had to be greatly extended for this to occur.

1.3.2.15 Roughead *et al*. (2009)

Roughead *et al*. recently undertook two retrospective cohort studies that investigated the effect of HMRs in Australian veterans using data from the DVA database. Although no economic analyses were undertaken in these studies, they are worthy of discussion as they are the only studies to associate HMRs with substantial reductions in the risk of hospitalisation. The first study investigated the outcomes of HMRs in veterans with heart failure.[174] They compared the time to next hospitalisation for heart failure in 273 veterans who received a HMR to 5444 veterans who did not receive a HMR. Participants were identified by having been dispensed a heart failure specific beta-blocker in the study period.

The study found a 37% reduction in rate of hospitalisation for heart failure at any time (HR 0.63; 95%CI 0.44-0.89) in the HMR group, and a 45% reduction (HR, 0.55 95% CI, 0.39-0.77) when adjusted for a number of co-variates. Whilst this finding suggests that HMRs are of major benefit in this population, there are many limitations to the study that mean it must be interpreted cautiously. These primarily result from some significant limitations in the dataset used for the analysis. The patient's co-morbidities were largely unknown: the number of co-morbidities was calculated from the number of medications dispensed, rather than counted from documented diagnoses.[x] Consequently, it is unknown how well matched the control and intervention groups

[x] this accounts for the reason why the study cohort was identified from having been dispensed a heart failure specific beta-blocker instead of from a diagnosis of heart failure as documented in their DVA client file

were. A second limitation involves the measurement of the study's only outcome. The researchers did not report how many hospitalisations were documented, so it is unclear to what extent this may have influenced the validity of the results.

1.3.2.16 Roughead *et al*. (2010)

The same database was used (and consequently the same limitations were present) in a second study by Roughead *et al*. who investigated the outcomes of HMRs in veterans taking warfarin.[175] They compared the time to next hospitalisation for bleeding in 816 veterans who received a HMR, to 16 320 veterans who did not receive a HMR.

Consistent with their heart failure study, the results were very positive for HMRs: when adjusted for a number of co-variates, the results showed a 79% reduction in likelihood of hospitalisation for bleeding between 2 and 6 months (HR, 0.21 95% CI, 0.05–0.87) in the HMR group. The unadjusted likelihood was not reported, and neither were the number of hospitalisations. Interestingly, the effect was not apparent in the 0 to 2 months post HMR, nor after 6 months post HMR. Furthermore, the HMR group were at increased risk of being hospitalised for bleeding more than 12 months after the HMR, compared to control.

The authors attributed their findings to the HMRs improving warfarin management in two different ways. They suggested that the delay in the time taken for the reduction in hospitalisations to become evident was due to a lag between the HMR occurring and the GP implementing the recommendations made by the pharmacist in the HMR report. Furthermore, they accounted for the loss of effect after 6 months being due to the educational benefits that were gained by the veterans during the HMR interview being lost after this time. Whilst these explanations seem plausible, there are some overt flaws in them.

Firstly, it may be argued that the benefits of patient education should be most evident when the education is first delivered, and so the two month lag before benefits were seen suggests that it was not education being lost that was responsible for the loss of effect after 6 months. Additionally, it is unclear as to why the benefits resulting from changes to medication regimens occurring because of HMRs would become insignificant after only 6 months. Many other studies of MMRs discussed in this

section failed to identify benefits resulting from MMRs in the 3 to 6 months after the MMR.[26, 66, 114, 147, 169] Consequently, several authors have recommended that follow-up periods in these studies should be substantially greater than 6 months for the full benefit of MMR interventions to become apparent![66, 114] It is possible that Roughead *et al*.'s interpretation of their results is correct, given the specificity of their study cohort compared to these other studies. However, if this is the case then it is unreasonable to extrapolate the findings to HMRs provided for all Australians.

A summary of the economic evaluations undertaken in the studies discussed in this section is presented in Table 14.

TABLE 14 - SUMMARY OF STUDIES INVESTIGATING ECONOMIC OUTCOMES OF MEDICATION REVIEWS UNDERTAKEN FOR PATIENTS LIVING IN THE COMMUNITY

STUDY	COUNTRY, DESIGN & PARTICIPANTS	INTERVENTION	ECONOMIC ANALYSIS & OUTCOME MEASURES	RESULTS	COMMENTS
Department of Veterans' Affairs Domiciliary Visit Evaluation (2000)[145]	Australia: retrospective observational cohort study; data from 92 patients who received MMR compared to 19 patients who did not.	Department of Veterans' Affairs medication reviews (similar to HMR; see text).	Partial CBA; cost of drugs, GP visits, MBS items and private hospital admissions.	Trend in increased number, but not cost, of drugs, in MMR group. Trend in increased health service costs in control group.	Limited documentation of many measured outcomes. All data obtained from DVA database; major limitations in drug usage analysis and hospitalisation data.
Zermansky *et al.* (2001) [146]	UK: RCT; 1188 patients aged ≥65 years randomised 1:1 to either medication review or usual care.	Clinical medication review performed at GP surgery.	CCA; cost and number of drugs, cost and frequency of health service use.	Intervention resulted in drug cost savings of £61 per patient per annum (P<0.05) compared to control; no increase in health resource use.	Limited economic evaluation. Reviews performed by a single pharmacist.
Krska *et al.* (2001) [46, 139]	UK: RCT; 332 patients aged ≥65 years with ≥2 chronic conditions taking ≥4 repeat prescriptions randomised to either i) MMR or ii) MMR and care plan.	Clinical medication review performed at patient's home. Control patients asked to address DRPs with GP; pharmacist provided care plan to GP in intervention group.	Partial CCA; only drugs costs measured. Number of health service visits counted but not costed. QOL.	NS differences between groups in drug costs, QOL and number of health service visits.	Limited economic evaluation. Both control and intervention groups received MMRs; study compared effect of care plans on outcomes of MMRs rather than MMRs to usual care.
Seniors Medication Assessment Research Trial (2003) [64, 150]	Canada: RCT; 889 patients aged ≥65 years taking ≥5 chronic medications randomised to either MMR (431 patients) or usual care (458 patients).	Clinical medication review performed at GP surgery.	CCA; drug and health service costs (see text). QOL.	NS differences between groups in drug costs, QOL and number of health service visits. Trend in reduced number of hospital stays in intervention group (P=0.08).	Limited economic evaluation; pharmacist time to perform intervention documented but not costed.
Evaluation of the HMR program (Pharmacy component) (2005) [15]	Australia: economic evaluation used a combination of a before-and-after study of 50 HMR recipients and results of two previous studies of HMRs. [86, 139]	HMR.	CUA; drug and health service costs obtained from previous studies. QOL.	HMR program offset costs entirely; resulted in savings to healthcare system of $4.5 million and 1425 QALYs country-wide.	Economic evaluation flawed due to incorrect costs used and questionable QOL measurement (see text).

STUDY	COUNTRY, DESIGN & PARTICIPANTS	INTERVENTION	ECONOMIC ANALYSIS & OUTCOME MEASURES	RESULTS	COMMENTS
Home-based Medication Review study (2005) [25, 26, 146-148]	UK: RCT; 889 patients aged ≥80 years randomised to either MMR (429 patients) or usual care (426 patients) following emergency hospital admission.	Clinical medication review performed at patient's home.	CBA; drug and health service costs. QOL.	30% more hospital admissions in MMR group (*P*=0.009). NS differences between groups in mortality or QOL; incremental cost per life year gained of £33 541 and £54 454 per QALY gained in intervention group.	Significant differences between groups in several baseline characteristics. Majority of hospital admissions in intervention group occurred in small number of patients.
POLYMED trial (2007) [169]	UK: RCT; 136 patients aged ≥80 years taking ≥4 chronic medications and at high risk of medication misadventure randomised to either MMR (69 patients) or usual care (67 patients).	Clinical medication review performed at patient's home.	Partial CA; only intervention costed. Number of non-elective hospital admissions and drugs reported but not costed. QOL.	NS differences between groups in number of hospitalisations or QOL. Reduced number of drugs in intervention group (-0.87, 95% CI -1.66 to -0.08, *P*=0.03). Intervention cost £112 per patient.	Limited economic evaluation. Reviews performed by a single pharmacist.
Community Pharmacy Medicines Management Project (2007) [23, 59, 170]	UK: RCT; 1493 adult patients with coronary heart disease randomised to either MMR (980 patients) or usual care (513 patients).	Clinical medication review performed at patient's home followed by further consultations as needed.	CMA; total NHS-related costs (including intervention). QOL.	NS differences between groups in any primary outcome measures. Total NHS-related costs (including cost of intervention) higher in intervention group (difference in medians £118.1 versus £97.4, *P*<0.0001).	Cost of intervention would have to be reduced by 35% for cost difference between intervention and control to become insignificant.
Denneboom *et al.* (2007) [162, 163]	Netherlands: RCT; 738 patients aged ≥75 years taking ≥5 chronic medications randomised to MMR with findings presented to GP by either i) case conference (387 patients) or ii) written feedback (351 patients).	Clinical medication review performed at patient's home.	Partial CA; intervention and drugs costed.	More medication changes in case conference group compared to written feedback group initially (*P*=0.02) and at 6 months after MMR (*P*=0.02), but not at 9 months (*P*=0.07). NS difference in total costs following MMR (*P*=0.655).	QOL not measured. Both control and intervention groups received MMRs; study compared effect of case conference versus written feedback on outcomes of MMRs rather than MMRs to usual care. Limited intervention cost data.

STUDY	COUNTRY, DESIGN & PARTICIPANTS	INTERVENTION	ECONOMIC ANALYSIS & OUTCOME MEASURES	RESULTS	COMMENTS
Altavela *et al.* (2008) [173]	USA: prospective controlled study; 343 patients aged ≥50 years with 1 or more high risk characteristics received MMR with findings either i) presented to GP (intervention group, 127 patients) or ii) not presented to GP (control group, 216 patients)	Clinical medication review performed at GP surgery followed by opportunistic additional counselling.	CA; health service and drug costs.	NS differences between groups in any cost. Trend in reduced emergency department visit costs in intervention group (P=0.054)	QOL not measured. Limited drug cost data. Cost of intervention not considered.

CA: cost analysis; CCA: cost consequence analysis; RCT: randomised control trial; CMA: cost minimisation analysis; CUA: cost-utility analysis; CBA: cost benefit analysis

1.3.2.17 Discussion

The results of Australian and international studies undertaken following the implementation of the HMR program do little to resolve the confusing findings of the five QUM implementation studies. In particular, they provide limited evidence that MMRs are clinically effective, and almost no evidence that MMRs are cost-effective. In consideration that the objective of HMRs is to "*improve quality of life and health outcomes*",[116] it may be argued that there is a need to investigate the outcomes of HMRs, and their cost-effectiveness.

These studies of MMRs provide some important insight into how further research into MMRs should be undertaken. In particular, they highlight several considerations regarding the outcomes that should be measured in such research, and the way in which these outcomes should be measured. An outcome that was frequently measured in the studies discussed in this chapter is hospitalisation. Most studies that investigated the effect of MMRs on hospitalisations used the total number of non-elective admissions, and found either no benefit,[64, 169, 173] or incongruously, increased admissions in the MMR groups compared to control.[26, 168] As discussed previously, it has been asserted by several researchers that preventable, drug-related hospitalisation is the most appropriate outcome measure for hospitalisations.[59, 64, 149] It is interesting to note that the two studies by Roughead *et al*. that associated significant reductions in hospitalisation with HMRs focussed on specific types of hospitalisations, many of which would have been at least in part drug-related.

A second conclusion that can be drawn from the studies discussed in this chapter is that MMRs do not appear to affect QOL in a way that is measurable with generic QOL instruments such as the EQ-5D and SF-36.[26, 66, 169] It has been said that these instruments are most suited to interventions that produce large changes in QOL in small numbers of patients (for example coronary stenting), as opposed to interventions such as MMR that result in small changes in large numbers of patients.[176] There is work being undertaken in developing a medicines-specific QOL instrument that may capture the benefits of MMR.[177] However, it seems likely that until such a tool is validated, there is little point in using generic QOL instruments, except to demonstrate that MMRs do not adversely affect QOL.

Finally, the maturity of the Australian HMR program adds another element of uncertainty to extrapolating the outcomes of many of the aforementioned studies to HMRs. It is possible that the long duration of the HMR program has influenced parameters that may affect the outcomes of HMRs, but are highly variable in short-term trials. These may include the level of inter-professional communication, endorsement by local groups or organisations, and expectations of the roles of the various types of healthcare professionals involved in the medication review process. To illustrate, Ballantyne commented that education to medical practitioners in the UK was required to improve the outcomes of studies of pharmacists' interventions to minimise drug-related harm.[178] As the HMR program has been in place for many years (and included the HMR facilitator program which aimed to perform this very task), it is of dubious validity to draw conclusion about HMRs from many studies of medication reviews. Hence, it is clear that there is a paucity of data regarding the clinical and cost-effectiveness of HMRs.

1.4 Economic evaluations

In this thesis thus far, the terms "cost-effective" and "economic evaluation" have been used frequently. It therefore seems prudent at this point to provide the reader with a brief introduction to the role of economic evaluations and the concept of cost-effectiveness.

1.4.1 Overview of economic evaluations

The science of economics evolved from the principle that resources (such as labour, capital and facilities) are scarce, and there will never be enough resources to completely satisfy human wants and needs. With regards to healthcare, society cannot afford to implement every possible intervention that improves health, so choices must be made between interventions. Health economics is a scientific discipline that applies economic principles to health and healthcare. A specific aspect of health economics involves the economic assessment of interventions to inform decisions made regarding the allocation of resources to and within the health economy. More succinctly, economic evaluations are conducted to assist decision makers to choose between alternative means of resource consumption.[135]

The term *economic evaluation* has been defined as *"the comparative analysis of alternative courses of action in terms of both their costs and their consequences"*.[135, 179] Implicit in this definition is that a true evaluation requires comparison; if no other alternative is considered then a program is simply *described.* In most economic evaluations, the comparator is chosen to reflect common clinical practice in the setting where the economic evaluation is undertaken.[180] For example, in an economic evaluation of a new drug therapy, the comparator may be an older drug, or if the new drug is the first of its kind then the relevant comparator may be no active therapy. In terms of economic evaluations of medication reviews, each study discussed in the previous sections compared medication reviews to usual care, as there was no competing intervention.

1.4.2 Types of economic evaluation

Several forms of economic evaluations have been described, although all have a common structure that requires explicit measurement of inputs ("costs") and outcomes ("benefits", also referred to as consequences) resulting from the intervention/s being investigated. Whilst there is some discordance between authors regarding the classification of types of economic evaluations,[135, 181, 182] six forms are frequently described in the literature. They are as follows: [183]

i. *Cost analysis*; where only the costs of the interventions being compared are considered, without measurement of outcomes.
ii. *Cost minimisation analysis* (CMA); which determines the least costly of two interventions whose outcomes are equivalent.
iii. *Cost-effectiveness analysis* (CEA); where the value of a single outcome of the interventions being compared is expressed in terms of a natural unit or physical (for example, cost per life saved). No monetary value is applied to the outcome, and the competing interventions must affect the same outcome.
iv. *Cost-utility analysis* (CUA); which is similar to CEA except that the outcome units do not have to be measured on the same natural scale. In CUA, outcome is measured in terms of patient wellbeing (termed utility), and hence theoretically allows the comparison of interventions across more than one field of medicine.

v. *Cost-benefit analysis* (CBA): in CBA, the outcome is not expressed in terms of natural units, but is assigned a monetary value, allowing comparisons across disease states. CBA can only be used when it is possible to determine a monetary value for benefits as well as costs.
vi. *Cost-consequence analysis* (CCA): in which costs and effects are calculated but not aggregated into quality-adjusted life-years (QALYs) or cost-effectiveness ratios. CCA is similar to CEA except that multiple outcomes are presented, allowing interpretation of the outcomes according to a decision-maker's own weighting system.

The choice of type of economic evaluation is determined by a number of factors, primarily relating to the characteristics of the intervention/s being assessed. For example, the outcome of the intervention/s may mean that a CBA cannot be performed if a monetary value cannot be assigned to the outcome of interest. Similarly, a CBA of a highly clinically effective new anti-migraine drug is unlikely to find it to be cost-effective, despite it substantially improving patients' quality of life.

In their review of the literature that investigated the cost-effectiveness medication reviews, Zermansky and Silcock identified numerous potential positive outcomes of such programs (Table 14). They asserted that either CBA or CUA is the most appropriate type of economic evaluation in this context as the most appropriate outcome to measure is utility, quantified in either monetary terms (if CBA) or QOL (if CUA). They further stated that the minimum requirement for an economic evaluation of medication reviews is one performed from a health service perspective and of at least one year's duration. However, their review concluded that few, if any, studies to date fulfilled these criteria.

TABLE 15 - DESIRABLE OUTCOMES OF MEDICATION REVIEWS LISTED BY ZERMANSKY AND SILCOCK[114]

PATIENTS			
• Reduce adverse effects	• Improve well-being	• Minimise expenditure	• Increase satisfaction with care
GOVERNMENT			
• Reduce inequalities	• Reduce hospitalisation	• Offer patient choice	• Reduce resource use
CLINICIANS			
• Save time	• Optimise effectiveness	• Reduce adverse effects	
OVERALL			
• Reduce mortality	• Improve quality of life	• Improve healthcare cost-effectiveness	

To date, the only Australian investigations into HMRs that calculated cost-effectiveness ratios were those undertaken by Sorensen *et al*. and the flawed 2005 Program evaluation.[15, 66] In the international literature, a cost-effectiveness ratio was reported only in the economic evaluation of the HOMER study.[25] There appears to be a clear need for further investigation into this aspect of the HMR program.

1.4.3 Definitions of cost-effectiveness

A useful concept when investigating cost-effectiveness using CBA and CUA is that of the cost-effectiveness plane, which graphically represents the differences in costs and outcomes for the interventions being assessed (Figure 4).[184] The horizontal axis represents the difference in effectiveness between the interventions being investigated, whilst the vertical axis portrays the difference in cost. The intervention being assessed will fall into one of four quadrants, labelled A to D.

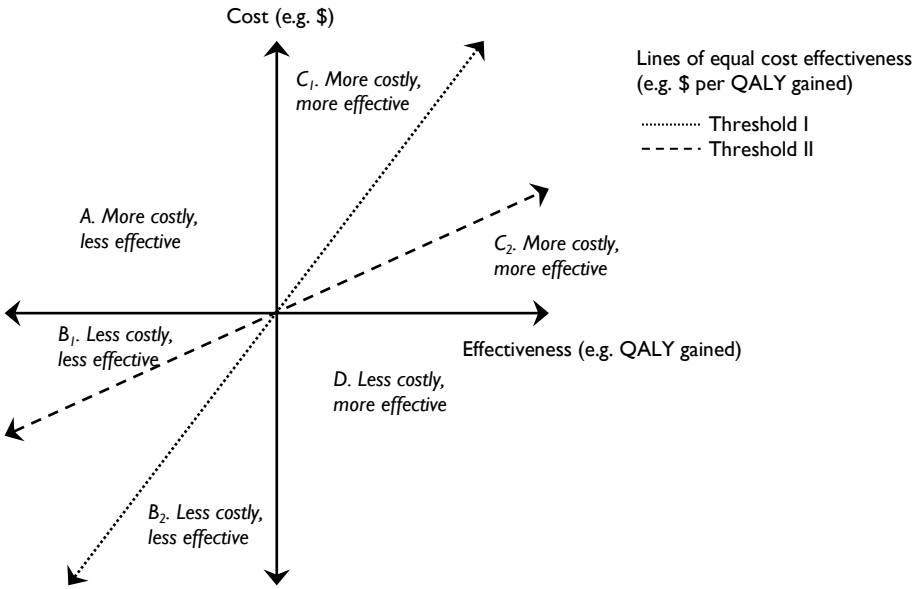

FIGURE 4 - DOMAINS ON THE COST-EFFECTIVENESS PLANE. DASHED LINE INDICATES COST-EFFECTIVENESS ACCEPTABILITY THRESHOLD

If the intervention is less effective and more costly (quadrant A) than the comparator, then it is said to be dominated by the comparator. This indicates that the intervention should not be adopted. Conversely, if the intervention is dominant (more effective and less costly than the comparator, falling into quadrant D), then it should be adopted. In both scenarios, there is no need to conduct an economic evaluation. However, should the intervention fall into quadrants B or C, then it may be considered cost-effective if it falls within a threshold of acceptance (sub quadrants C_2 and B_2). Notably, cost-effectiveness is an arbitrary threshold and may vary according to a multitude of circumstances. In Figure 4, two different thresholds of cost-effectiveness are shown to illustrate this. For both thresholds, the region below the line may be considered cost-effective, and the region above not cost-effective.

There are numerous thresholds of acceptance in use worldwide. The World Health Organisation CHOosing Interventions that are Cost-effective (WHO-CHOICE) defines three categories of cost-effectiveness based on a country's GDP per QALY gained:

- Highly cost-effective (less than GDP per capita);

- Cost-effective (between one and three times GDP per capita); and
- Not cost-effective (more than three times GDP per capita).[185]

These thresholds are by no means absolute with regards to most countries' healthcare systems, including that of Australia. For example, Australian GDP per capita in 2008 was approximately $48 500. The Pharmaceutical Benefits Advisory Committee has recommended drugs for government subsidy at higher thresholds than $48 500 per QALY gained, although has been found to be unlikely to do so if the cost exceeded $76 000.[186] In the UK, the National Institute for Health and Clinical Excellence (NICE) uses a threshold of £20 000 to £30 000 per QALY, and in the US, a threshold of US$ 50 000 to $100 000 per QALY is often is mentioned in medical literature.[187] By not using explicit thresholds, a degree of arbitrariness is permitted, which may be more attractive to policy decision-makers.[188]

1.5 Conclusions

Having reviewed the relevant literature, it is apparent that firm conclusions about the efficacy, effectiveness and cost-effectiveness of HMRs cannot be made. Whilst there is considerable evidence that pharmacists identify and make recommendations to resolve or prevent DRPs in the high-risk populations investigated in most studies, the outcomes of them addressing DRPs in medication reviews is unclear. The results of the studies reviewed in this chapter have important ramifications for the Australian HMR program, in particular raising questions as to whether HMRs are realising the clinical and economic outcomes reported in the QUM evaluation studies. There is a clear need for research into the clinical and cost-effectiveness of HMRs. In particular, there is a need for a well-designed and detailed cost-effectiveness analysis.

1.6 Aims and objectives

Based on the literature, it was hypothesised that HMRs are not cost-effective compared to usual care; hence the overall aim of the research described in this thesis was to investigate the clinical and cost-effectiveness of HMRs. To achieve this aim, the following objectives were formulated and addressed:

- To investigate novel methods for assessing the clinical and cost-effectiveness of HMRs;
- To investigate the characteristics of the DRPs identified in HMRs, including the drugs and conditions involved, and the recommendations made to resolve or prevent DRPs;
- To estimate the clinical effectiveness and cost-effectiveness of HMRs; and
- To investigate potential avenues to optimise the clinical effectiveness and cost-effectiveness of HMRs.

Chapter 2 - General methods

2.1 Overview

2.1.1 Study design

The study was initially conceived as a RCT, similar to that undertaken by Sorensen *et al*.[66] Such a study would need to be powered sufficiently to detect changes in multiple health resource parameters over a period of at least 12 months. However, this approach presented several challenges. Firstly, in consideration of the number of parameters that would need to be measured per patient, data collection would have been extremely time-consuming. Secondly, as demonstrated by Holland *et al*.,[26] in such studies, a small number of patients may incur large costs and skew the results. Similarly, the QUMCIT identified that the majority of cost savings resulting from HMRs were most likely to occur from reductions in hospitalisation in small numbers of patients.[126]

In consideration of this, the number of subjects required for a study to detect a conservative 10% reduction in hospitalisation in older adults was calculated. Burgess *et al*. identified that the annual hospitalisation rate due to ADEs in elderly Australians was approximately 12.9 per 1000 person-years in 2002.[11] A RCT would therefore require over 1500 patients in both the intervention and control groups to detect a 10% reduction in hospitalisations resulting from ADRs at a power of 90% ($P<0.05$). However, only a portion of these hospitalisations are potentially preventable, so the actual sample size would need to be substantially larger. To further illustrate this issue, a cluster randomised, controlled multi-centre study of medication reviews in the Netherlands is currently underway.[189] The sample size for this study was based on an assumption that medication review would reduce *medication-related* hospitalisation by 50%. The study aimed to enrol 14 200 patients who were randomised on a 1:1 basis to receive either medication review or usual care. Such a study was outside the scope of the available budget and timeline, as such it was concluded that an RCT was not a plausible design for the study.

A further complication was introduced by the widespread availability of HMRs limiting the recruitment of a suitable control group. Greenhill found that a HMR

performed for a patient of one GP may result in changes occurring in several other patients under that GP's care, so randomisation undertaken on a per-patient patient basis was inappropriate.[136] As a result, it would have been necessary to randomise patients per GP or GP practice, as had been done in several previous studies.[64, 66] However, conducting the trial in this way would have necessitated some patients being ineligible to receive HMRs, which may potentially have been viewed as ethically questionable in consideration that there is some evidence of benefit.[190]

These issues were not unique to the investigation of HMRs. To undertake any impact evaluation, an assessment of the consequences of patients not receiving the intervention is preferred. A related field in which RCTs are rarely, if ever, undertaken, involves clinical interventions performed during community pharmacy practice.[191] A further concern in this field, in addition to ethical issues, is that pharmacists are professionally obliged to perform clinical interventions. Hence, it is not plausible to control studies of these interventions with a group that receives no intervention.

Consequently, several previous studies have evaluated the potential clinical and economic outcomes of pharmacists' clinical interventions through the use of expert opinion to estimate the counterfactual state, that is, what would have happened had the clinical interventions not occurred.[192-201] In general, these studies involved experts predicting the health outcomes that would have occurred with and without the intervention to generate estimates of the effect of the intervention. A similar approach was taken in the QUMCIT and Sutherland project. In these studies, expert opinion was used to estimate the clinical outcomes and their associated costs to compare the effect of the intervention (the HMR) to the same patient not receiving the intervention.[86, 126, 138-140]

Consequently, an uncontrolled observational cohort study was undertaken, and the methodology used is described in detail on page 92. Briefly, four projects were undertaken to achieve the overall aim of the research described in this thesis. The first two studies involved evaluating the potential costs and QOL effects associated with specific DRPs. The outcomes of these two studies were then used to evaluate a sample of HMRs to estimate the clinical and economic outcomes resulting from HMRs. Finally, a sample of these HMRs were further analysed to identify potential predictors of cost-effectiveness. This is illustrated in Figure 5.

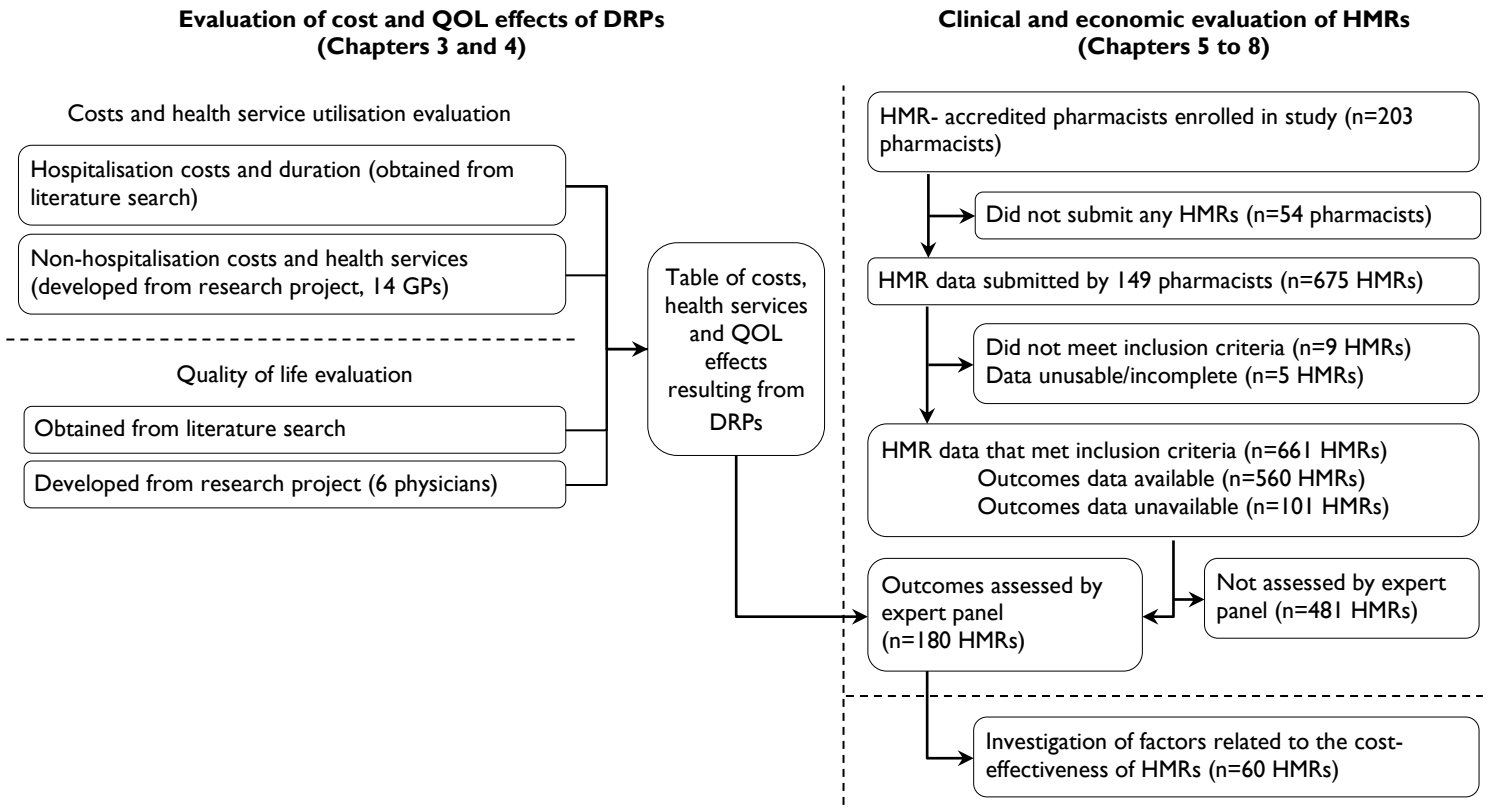

FIGURE 1 - FLOW CHART ILLUSTRATING RESEARCH STUDIES DESCRIBED IN THIS THESIS. DASHED LINES DELINEATE THE DISCRETE STUDIES UNDERTAKEN

2.1.2 Outcome measures

There were three primary outcomes for the study. These were:

- the number of DRPs;
- QOL; and
- costs.

QOL and costs were included to allow the planned economic evaluation. Secondary outcomes were as follows:

- the type, frequency and drugs involved in the DRPs;
- the recommendations made by the pharmacists to prevent or resolve the DRPs;
- the uptake of the recommendations made by the pharmacists.

Given the focus of the study on the resolution of DRPs, the unit of analysis was the DRP, as opposed to the recommendation.

2.1.3 Data collection

2.1.3.1 Patient characteristics and DRPs identified

There were three sources from which data were collected to characterise each patient who received a HMR, the DRPs identified by the reviewing pharmacist, and the outcomes of the recommendations made in the HMR. These were:

- the HMR referral from the GP;
- the HMR report from the accredited pharmacist who performed the review; and
- data regarding whether the recommendations made in the HMR report were enacted upon by the GP or not (i.e., the outcomes of the HMR).

The data obtained from these sources are shown in Table 16.

TABLE 16 - SOURCES AND TYPES OF DATA COLLECTED FOR EACH HMR

DATA SOURCE	DATA COLLECTED
HMR referral	Reason for referral Patient demographics (age, sex, medical conditions) Pathology/ laboratory data Medication profile
HMR report	DRPs identified Recommendations
Outcomes	GP acceptance or rejection of pharmacists' recommendations

All patient diagnoses and medical conditions were classified using the International Classification of Primary Care Version 2 PLUS (ICPC2-PLUS, Family Medicine Research Centre, University of Sydney).[202] Patient medications were recorded using Anatomic Therapeutic Chemical (ATC, World Health Organisation) coding.

All data relating to the HMRs analysed was submitted by the accredited pharmacist who performed the HMR. Accredited pharmacists were asked to submit details pertaining to HMRs that they performed between March and November of 2008. To reduce the possibility of selection bias, participating pharmacists were requested to submit details of sequentially the next five HMRs they performed after enrolling in the study. The pharmacist enrolment/ consent to participate form is shown in Appendix II.

It was envisaged that outcomes data would be readily available from the medication management plan formulated by the GP following the HMR. If no medication management plan was received, then the pharmacist was asked to contact the GP directly and obtain the relevant outcome data using a "Outcomes summary" form (Appendix III). It is noteworthy that the "Outcomes" in Table 16 only included the DRPs that required the GP to accept and implement the pharmacists' recommendation/s to resolve. It was envisaged that many DRPs would have been resolved by the pharmacist without requiring the GP's direct involvement. A limitation of this design is that, whilst the GP may have agreed with the pharmacist's assessment and recommendation to resolve a DRP, the patient may not have agreed to the changes suggested. Hence, what actually happened may not have been captured using the "Outcomes summary" form.

Outcome data was not collected for every recommendation made by the pharmacist. Previous research suggested that the mean number of DRPs that would be identified in the VALMER study would be between two and five (Table 2). Anecdotal evidence from experienced accredited pharmacists indicated that the acceptance of recommendations made in HMRs diminishes as the number of recommendations increases. Additionally, it was considered that most pharmacists prioritise the DRPs identified in HMRs from most to least clinically relevant. Consequently, data regarding the outcomes of the first three recommendations made by the pharmacist in the HMR report was collected by the accredited pharmacist who performed the HMR. It was planned that these data would be used to provide an indication as to the outcomes of the recommendations made in the HMR report with the greatest potential to improve patient health and reduce health resource utilisation. The limitations resulting from this approach are discussed in detail in Section 7.3.1.2.

To create awareness of the project and facilitate its promotion, the acronym VALMER (the Economic Value of Home Medicines Reviews) was used. Throughout this thesis, VALMER is used to describe the study that was undertaken to investigate the clinical and economic outcomes of HMRs. The results of the VALMER study are presented in chapters 5 and 6.

2.1.3.2 Inclusion and exclusion criteria

Any HMR undertaken in the data-collection phase of the study was eligible for inclusion. The only criteria for exclusion from the study were as follows:

- HMR performed outside of the data collection phase (due to an increased risk of HMR selection by the submitting pharmacist);
- incomplete or missing referral or HMR report data.

2.1.3.3 Pharmacist recruitment

Accredited pharmacists were recruited using advertisements in a variety of professional pharmacy-specific media. Advertisements were published in *Australian Pharmacist*, *Australian Journal of Pharmacy* and *The Accredited Pharmacist* magazines (an example may be found in Appendix IV), and a media release was distributed by the

Pharmacy Guild of Australia (Appendix V). The project was also promoted at the three largest accredited pharmacist-specific continuing education events in 2008., which were:

- the accredited pharmacist forum at the Australian Professional Pharmacy Conference, Gold Coast, Queensland (27 March 2008);
- the AACP Consultant Pharmacy Clinical Seminar, Adelaide (29 May-1 June 2008); and
- the accredited pharmacist forum at the Pharmacy Australia Congress, Perth (24 October 2008).

The website www.valmer.com.au was also used to promote the study, and serve as a resource for participants to download the materials required for participation and newsletters containing project updates (Appendix VI).

2.2 Pharmacist characteristics

The pharmacists who participated in the VALMER study by submitting HMRs were characterised in two ways. They completed a survey that described their general demographics, and their clinical knowledge was assessed using their score for the AACP accreditation and reaccreditation examinations.

2.2.1 General demographics

The characteristics of the pharmacists who participated in the VALMER study were assessed with an online survey that was distributed in April 2009 (Appendix VII). The survey covered the following aspects of the pharmacists' training and practice:

- education history (undergraduate, postgraduate and professional development);
- years of experience in different areas of pharmacy practice;
- current employment status;
- number of HMRs and RMMRs performed and years of experience performing MMRs;
- attitudes towards the HMR processes; and

- use of software when performing MMRs.

2.2.2 Clinical performance

As discussed in Section 1.2.2.3 (page 24), all pharmacists must successfully complete a 50-question multiple-choice examination to initially achieve MMR accreditation with AACP. Once accredited, they must then pass this assessment every three years.[129] The minimum pass score for the examination is 74% (37 correct responses out of 50). The AACP states that the assessment has been designed to assess "*competence in clinical pharmacy, therapeutics, pharmaceutical care and medication review…* <focussing on> *knowledge of the principles of geriatric medicine, rational and safe pharmacotherapy in the elderly, and the appropriate use and interpretation of laboratory tests*".[129]

This examination was used to provide an indication of the clinical knowledge of the pharmacists who participated in the VALMER study. The AACP provided examination scores for every pharmacist who sat this examination between March 2007 and June 2009. This allowed a number of investigations to be made, including:

- comparisons between the scores of the pharmacists who participated in the VALMER study with those of all pharmacists who undertook the assessment to investigate whether the VALMER pharmacists were representative of all AACP-accredited pharmacists in terms of clinical knowledge; and
- whether the pharmacists' clinical knowledge was related to the cost-effectiveness of their medication reviews.

2.3 Drug-related problems

The studies discussed in Chapter One of this thesis demonstrated that there is considerable uncertainty regarding the outcomes resulting from the identification and resolution or prevention of DRPs in MMRs. However, it seems that the *type* of DRPs identified in medication reviews is somewhat related to their cost-effectiveness. Furthermore, several authors have asserted that any assessment of medication reviews must include documentation of the types of DRPs that were addressed in the reviews.[151, 166]

In consideration of this, every DRP documented in the HMR reports was classified using a version of a classification system that had been developed specifically for use in HMRs, called the DOCUMENT classification system.[203] This was a derivative of a system that has been used and refined in three studies spanning 10 years of research into DRP detection and resolution by Australian community pharmacists.[50] Using this hierarchal DRP classification system, the following aspects of each DRP were recorded: the characteristics of the DRP (type and subtype, drugs and medical conditions involved); the recommendations made to resolve or prevent the DRP, and the outcomes of the recommendations. All classification was undertaken by the researcher rather than the reviewing pharmacist to ameliorate inter-rater inconsistencies, which are common in DRP classification.[48]

2.3.1 DRP characteristics

The DOCUMENT system is a two-tiered hierarchical classification that defines 38 subtypes of DRP, grouped into 8 DRP types (Table 17).

TABLE 17 - TYPE AND SUBTYPES OF DRPS DEFINED BY THE DOCUMENT CLASSIFICATION SYSTEM [203]

TYPE OF DRP	SUBTYPE OF DRP
Drug selection *Problems related to the choice of drug prescribed or taken*	Duplication Drug interaction Wrong drug Wrong dosage form Unnecessary therapy/no apparent current indication Contraindications apparent Other drug selection problem
Over- or under-dose prescribed *Problems related to the prescribed dose or schedule of the drug*	Dose too high Dose too low Other Dose Problem
Compliance *Problems related to the way the patient takes their medication*	Taking too little Taking too much Intentional drug misuse Difficulty using dosage form Patient using out of date medication Other Compliance Problem
Untreated indications *Problems relating to actual or potential conditions that require management*	Condition not adequately treated Therapy required Other Untreated indication Problem
Monitoring *Problems relating to monitoring the efficacy or adverse effects of a drug or patient conditions*	Laboratory Monitoring Non-Laboratory monitoring Other Monitoring Problem
Education or Information *Problems relating to knowledge of disease or its management*	Patient drug information request Confusion about therapy Demonstration of device Disease management or advice Other Education or Information Problem
Non-clinical *Problems involving aspects of patient therapy that may not be directly related to drug therapy, such as lifestyle issues*	Weight management problem Dietary problem Exercise problem Smoking problem Alcohol problem Caffeine problem Other non-clinical problem
Toxicity or Adverse reaction *Problems relating to the presence of signs or symptoms which are suspected to be related to an adverse effect of the drug*	Toxicity caused by dose Toxicity caused by drug interaction Toxicity evident Other Toxicity/Adverse Effect problem

In addition to classifying and recording the type and subtype of each DRP, the drug/s and medical condition/s or symptom/s involved in each DRP were also documented. For example, a DRP involving a patient taking digoxin who was experiencing nausea was classified as a *Toxicity evident* subtype of DRP, with the drug *digoxin* and symptom of *nausea* tagged to the DRP. This allowed characterisation and analysis of the DRPs according to the drug/s and condition/s involved in the DRP, in addition to the types of DRP.

2.3.2 Recommendations and outcomes

Recommendations made by the pharmacists to resolve or prevent the DRPs documented in the HMR reports were classified according to the 15 category DOCUMENT system (Table 18). As with the DRP classifications, the recommendations are grouped into different types.

TABLE 18 - CATEGORIES OF RECOMMENDATIONS DEFINED BY THE DOCUMENT CLASSIFICATION SYSTEM [203]

TYPE OF RECOMMENDATION	SUBTYPE OF RECOMMENDATION
Drug therapy change *When the pharmacist recommended a change to the patient's drug therapy*	Dose increase Dose decrease Drug cease Drug start Formulation change Dose schedule change Drug switch Other therapy change
Education *When the pharmacist provided written or verbal education to resolve an identified DRP*	Patient/carer education Prescriber information Compliance assistance
Monitoring *Problems relating to monitoring the efficacy or adverse effects of a drug or patient conditions*	Laboratory Monitoring Non-Laboratory monitoring
Follow-up *When a DRP was identified, but the pharmacist made a recommendation of further investigation that was not related to monitoring*	Follow-up by prescriber Follow-up by another
Absence of a recommendation *When no recommendation is made regarding an identified DRP*	No recommendation necessary No recommendation made

The outcome of every recommendation was also classified according to the categories defined by the DOCUMENT system (Table 19).

TABLE 19 - OUTCOMES DEFINED BY THE DOCUMENT CLASSIFICATION SYSTEM
203

TYPE OF OUTCOME	DESCRIPTION OF OUTCOME
Recommendation totally accepted	*When the recommendation was totally accepted by the prescriber and the suggested change was implemented in full*
Recommendation partially accepted	*When the recommendation was accepted by the prescriber but only part of the suggested change was implemented*
Recommendation not accepted	*When the recommendation was rejected by the prescriber and no changes were implemented*
No acceptance necessary	*When the recommendation required no action by the GP for implementation in full*
Different resolution	*When the prescriber rejected the recommendation made by the pharmacist but made changes to resolve the DRP in an alternative way*
Unknown	*When it is not known if the prescriber accepted or rejected the recommendation made by the pharmacist*

Comprehensive scope notes and usage instructions for the DOCUMENT system are provided in Appendix VIII.

2.4 Economic protocol

An important aspect of an economic evaluation is the protocol used to undertake the evaluation. In designing the methodology of the economic evaluation for the study, substantial consideration was given to addressing the ten elements of a sound economic evaluation as defined by Drummond *et al.*, and shown in Table 20.[135] The following section describes the considerations made in this study to ensure that each of these facets was addressed appropriately.

TABLE 20 - CHECKLIST FOR ASSESSING ECONOMIC EVALUATIONS. FROM DRUMMOND *ET AL.*[135]

1.	Was a well-defined question posed in an answerable form?	6.	Was a comprehensive description of the competing alternatives given?
2.	Was the effectiveness of the programmes or services established?	7.	Were all the important and relevant costs and consequences for each alternative identified?
3.	Were costs and consequences measured accurately in appropriate physical units?	8.	Were costs and consequences valued credibly?
4.	Were costs and consequences adjusted for differential timing?	9.	Was an incremental analysis of costs and consequences of alternatives performed?
5.	Was allowance made for uncertainty in the estimates of costs and consequences?	10.	Did the presentation and discussion of study results include all issues of concern to users?

2.4.1 Research question and study perspective

In their review of studies that investigated the cost-effectiveness of MMRs, Zermansky and Silcock stated that the objective of an economic evaluation of any MMR program should be to establish whether the program is an appropriate use of resources compared to all possible alternatives for the same patient group.[114] Based on this objective, they asserted that the minimum requirement for an economic evaluation is a determination of the costs and consequences clearly associated with MMRs over a 1-year period from a health service perspective.

Therefore, a health sector perspective was adopted for the VALMER study, with the major focus on the impact for government as a third-party funder. To allow comparisons between competing interventions, the most appropriate outcome for this study was utility, quantified in either monetary terms (i.e. CBA) or as QOL (i.e. CUA).

The economic evaluation aimed to answer the question, *"From the viewpoint of the Australian government, is the HMR program cost-effective in addressing DRPs, compared to the cost of not addressing them?"*.

The next consideration involved identifying and quantifying the relevant costs.

2.4.2 Costs

A fundamental component of any economic evaluation is measurement or estimation of the mean costs of each treatment option. A cost may be defined as the value of resources consumed by undertaking the treatment option.[179] In most evaluations, this includes both input costs (such as the cost of renumerating pharmacists for providing HMRs) but also the cost savings resulting from the prevention of ill health (such as hospitalisations resulting from ADEs). Drummond *et al.* identified three general stages in estimating costs in economic evaluations:[135]

i. identification of relevant resources;
ii. estimation of resources consumed; and
iii. valuation of these resources.

These three stages are discussed in detail in the following sections.

2.4.2.1 Identification of resources

The resources that may be consumed as a result of medication review have been well-defined in previous studies. A summary of these relevant resources was published by Zermansky and Silcock,[114] and is shown in Table 21.

TABLE 21 - RESOURCES POTENTIALLY AFFECTED BY PROVISION OF MEDICATION REIVEWS. REPRODUCED FROM ZERMANSKY AND SILCOCK [114]

STAFF	SPACE AND EQUIPMENT	CONSUMABLES
Pharmacist time [a]	Consulting rooms [a]	Medicines (purchase) [a]
Doctor time (primary care) [b]	Transport (capital) [a]	Medicines (dispensing) [a]
Nurse time [c]	Hospital admissions [a]	Diagnostic tests [a]
Specialist time [c]	Theatre time [c]	Stationery [a]
Patient time during review [a,d]	Out-patient follow-up [c]	Transport (running costs) [a]
Loss of earnings [c,d]	Medicine storage [a,d]	Co-payments or fees [a,d]

[a] Items most directly linked to the process of review.

[b] Number of consultations is easily and reliably measured.

[c] Costs are generally less likely to be measured or accurately predicted, and are associated with longer-term consequences.

[d] Borne by patient.

The perspective of an economic evaluation determines which of these resources should be considered.[180] As a health sector perspective was chosen for the study, the relevant resources were those subsidised by the Australian Government, and are shown in Table 22. These resources are consistent with those assessed in several previous studies of HMRs discussed in Chapter One, section 1.3.1.[66, 126, 139]

TABLE 22 - RELEVANT RESOURCES IN THE VALMER STUDY

COST OF PROVIDING THE HMR	HEALTH RESOURCE UTILISATION	
Reimbursement to community pharmacy/ pharmacist	Drug costs	Hospitalisations
Reimbursement to GP	GP visits	Laboratory tests
	Specialist visits	

Having identified the relevant resources, the next consideration was the technique used to measure their consumption.

2.4.2.2 Estimation of resource consumption

2.4.2.2.1 Cost of providing the HMR

As discussed in Section 1.2.2.4, the funding model for HMRs involves reimbursement by Medicare Australia for both the community pharmacy and GP. There is no separate patient co-payment.[xi] For the purposes of this study, it was assumed that both the pharmacy and GP would claim for each HMR (that is, they would not forget or choose to not claim for their involvement). It was considered that this was the most conservative assumption regarding this cost, and the most risk averse from the government's perspective, as per the economic protocol.

The amount received by a GP for their involvement in a HMR is fixed. In contrast, rural pharmacies may be eligible for an additional travel allowance between $10 and $60 per HMR if the pharmacist must travel greater than 10km from the pharmacy to the patient's residence. Information was requested from Medicare Australia to account for this loading; however it was not provided. It was therefore assumed that no rural loading was applied to any HMR in the baseline scenario. This assumption was investigated in the scenario analyses, described in section 2.4.4 of this chapter.

In consideration of the cessation of the HMR facilitator program in the Fifth Community Pharmacy Agreement in 2010,[18] no costs associated with promoting the program were considered.

2.4.2.2.2 Health resource utilisation

2.4.2.2.2.1 Measurement considerations

Two methods of resource measurement were considered to estimate health resource utilisation, namely direct measurement and modelling using expert opinion. Direct measurement would have ideally involved the study being of a randomised controlled design, similar to that undertaken by Sorensen *et al*.[66] However, this was not

[xi] A patient cost may only be incurred if their GP does not bulk-bill during the follow-up consultation

considered feasible in consideration of the required sample size, as previously discussed.

The second method considered for estimating resource usage was the use of expert opinion, as used by both Gilbert *et al*. and Krass *et al*. in their QUM Evaluation Projects.[126, 139] Both studies used methods based on work by Rupp and Buurma whereby panels of experts were used to value interventions undertaken in community pharmacies.[193, 198, 199] These studies involved counterfactual impact evaluation, whereby the experts were asked to predict what would have happened to the patient had the intervention not occurred, in terms of health resource consumption such as hospitalisation or GP involvement. This type of evaluation was used in preference to a controlled design due to ethical issues in denying patients standard practice for the purposes of evaluating it.

Recently, Tenni identified several deficiencies in the Rupp and Buurma methods (and consequently the studies by Gilbert *et al*. and Krass *et al*.) that limited the robustness of results obtained using them.[204] These included their methods not accounting for:

1. potential detrimental effects of the intervention (that is, adverse effects may result from an intervention, as well as beneficial effects);
2. multiple potential consequences resulting from the same intervention (as opposed to a single "most likely" or "most valuable" consequence); and
3. another party undertaking the same intervention (most patients see multiple healthcare providers therefore there are many opportunities for the same intervention to be undertaken).[204]

To overcome these issues, Tenni (as described by Stafford *et al*., Appendix IX)[191] developed a technique whereby experts assigned probabilities to several potential outcomes before and after an intervention.[204] Moreover, the experts also indicated the likelihood of another party undertaking the same intervention to ameliorate the third issue described above.

It must be acknowledged that economic analyses performed using expert panels provide a lower level of evidence compared with studies where empirical data is collected, such as in randomised- or case- controlled studies.[205] However, it has been

argued that expert opinion may be useful in areas where there is uncertainty, controversy or incomplete evidence,[205] and the results of studies that have used expert panels should not be summarily dismissed.[206] Given that the methodology developed by Tenni sought to improve the robustness of expert panel results, it was considered that this methodology was the most appropriate to estimate resource consumption for this study.

An overview of Tenni's methodology is presented in the following section.

2.4.2.2.2.2 Methodology overview

Methodological framework

A conceptual model of Tenni's methodology is shown in Figure 6. The model considers that three potential scenarios may occur when a DRP is present:

1. the DRP is not identified by the pharmacist nor anyone else involved in managing the patient;
2. the DRP is not identified by a pharmacist but is identified and addressed by another person involved in managing the patient's health; or
3. the DRP is identified and addressed by a pharmacist.

In all scenarios, numerous health consequences (both beneficial and detrimental) may potentially result from either the DRP or its resolution. However, for the purposes of evaluating the pharmacist's involvement in the patient's management, only the effects resulting from Scenario 3 can be attributed to the pharmacist. The consequences of Scenarios 1 and 2 would occur regardless of whether the pharmacist was involved in the patient's care and therefore become the counterfactual.

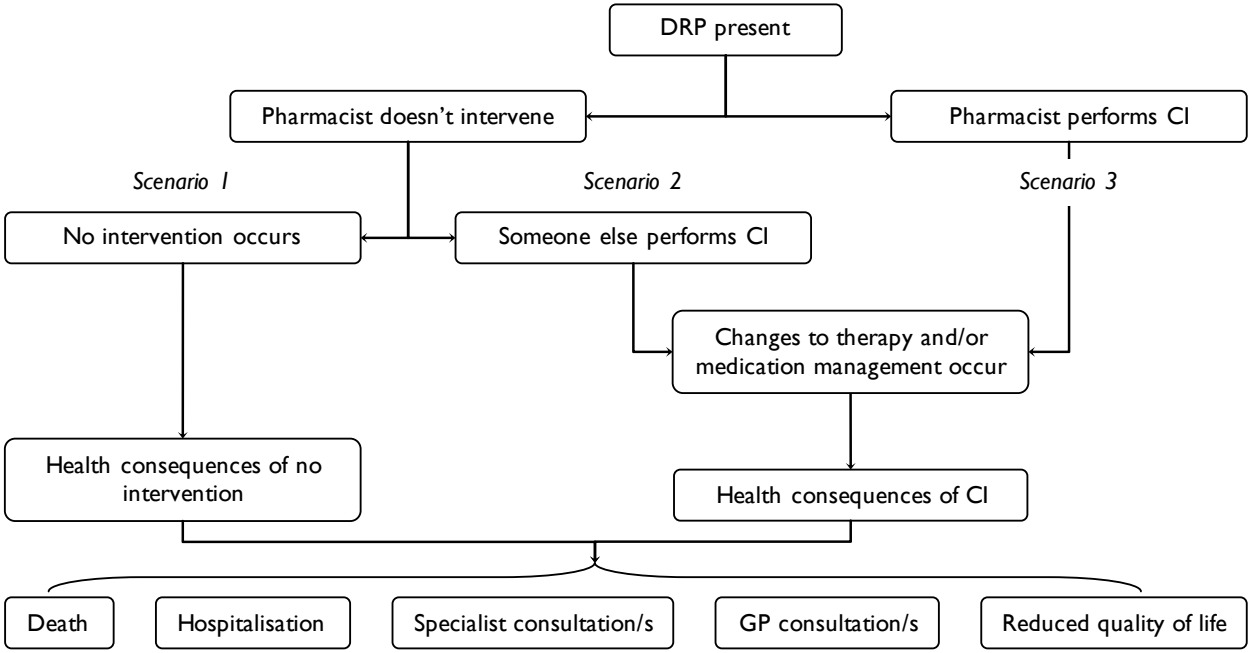

FIGURE 6 - CONCEPTUAL MODEL FOR ESTIMATING THE IMPACT OF PHARMACISTS' CLINICAL INTERVENTIONS ON HEALTH SERVICE UTILISATION AND QUALITY OF LIFE. "CI" INDICATES CLINICAL INTERVENTION. REPRODUCED FROM STAFFORD *ET AL.*[191]

Tenni's methodology involved experts predicting several parameters to provide an estimate of the clinical and economic value of resolving a DRP. Essentially, the experts predict:

- the potential consequences that may occur in the absence of any intervention (Scenario 1);
- the likelihood of another party performing the intervention (Scenario 2);
- the potential consequences that may occur because of the intervention (Scenarios 2 and 3);
- the probability of these consequences occurring before and after the intervention (Scenarios 1, 2 and 3); and
- the outcomes resulting from each consequence occurring at each level of severity, in the absence and presence of the intervention.

Consequences of an intervention

To simplify the expert assessment process, Tenni formulated a list of common consequences referred to as the "Consequences table". A comprehensive review of the Consequences table is presented in Chapter Three of this thesis. Briefly, the costs of the health resources (or other parameters) that would be expected to be incurred should the consequence occur were linked to each consequence. To predict the outcomes of an intervention, experts selected any number of consequences they considered plausible from the consequences table. Once the expert selected their desired consequence/s, they then estimated the change in risk for each chosen consequence. These estimates were then multiplied with the health resource utilisation parameters assigned to the consequence, to generate an estimate of the cost or savings resulting from the intervention.

A unique feature of Tenni's methodology compared to those developed by Rupp and Buurma is that it allows the expert to consider each consequence occurring at three different levels of severity termed health states- *Mild*, *Moderate* and *Severe*, Figure 7. To illustrate the need for considering different severity levels of the same consequence, consider the following example:

> *A pharmacist discovers that a patient who has recently experienced a myocardial infarction has ceased their antiplatelet therapy as they believed it was only required for short term use. The pharmacist confirms that the patient should remain on an antiplatelet agent and the patient recommences it.*

There were several consequences, both beneficial and detrimental, that potentially resulted from this intervention. One potential beneficial consequence is a reduction in the risk of recurrent myocardial ischaemia. Conversely, a potential detrimental consequence was an increase in the risk of bleeding as an adverse reaction to the antiplatelet drug. The severity of bleeding may have ranged from a minor bleed of little clinical significance to major bleeding requiring hospitalisation and substantial medical care. Moreover, the probability of each consequence occurring at different severity levels may also have been different. In this example, it was likely that the probability of minor bleeding occurring would have been much higher than the likelihood of major bleeding.[207]

Tenni's methodology involved each expert selecting any plausible consequence/s they considered could result from the DRP, then estimating the change in risk for each chosen consequence. Each consequence was graded into three separate health states, and the probability of each health state occurring was different. In the previous example, the severity of bleeding may have ranged from a minor bleed of little clinical significance to major bleeding requiring hospitalisation and substantial medical care. Therefore, each expert considered not only the probable consequences of the intervention, but also the relative probabilities of these consequences occurring at different severity levels (Figure 7).

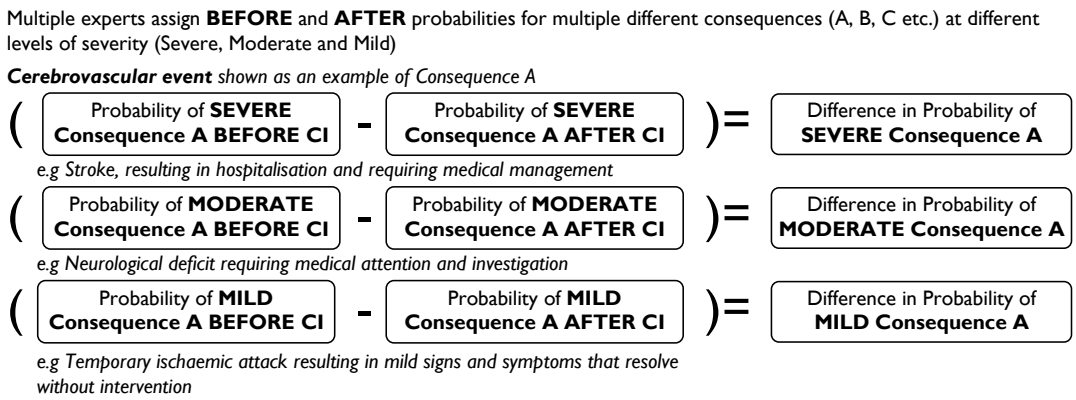

FIGURE 7 - DETERMINATION OF DIFFERENCE IN PROBABILITY OF DIFFERENT CONSEQUENCES. "CI" INDICATES CLINICAL INTERVENTION. REPRODUCED FROM STAFFORD *ET AL.*[191]

An additional benefit of Tenni's approach is that it partially ameliorates the requirement for a large sample size. For events to be detected in RCTs they must actually occur; for example, a hospitalisation, a visit to the GP *et cetera*. In contrast, by obtaining probabilities, the likelihood for each patient to experience the event is measured, so the event does not actually have to occur for it to be accounted for.

Calculation of total value

To calculate the absolute change in risk of each consequence occurring using this methodology, the expert's predictions of the before- and after- intervention probabilities of each consequence were used. For example, assuming a 12-month time horizon, if the expert had indicated that there was a 3% chance of a severe stroke before the intervention and a 1% chance of a severe stroke after the intervention, then this would reflect an absolute 2% reduction in the chance of a severe stroke.

At this stage, once the experts had selected the relevant consequences and assigned before- and after- probabilities to them, the total value of the intervention was calculated (Figure 8). The value of the intervention was in terms of the parameters assigned to each consequence, such as hospitalisation costs and duration.

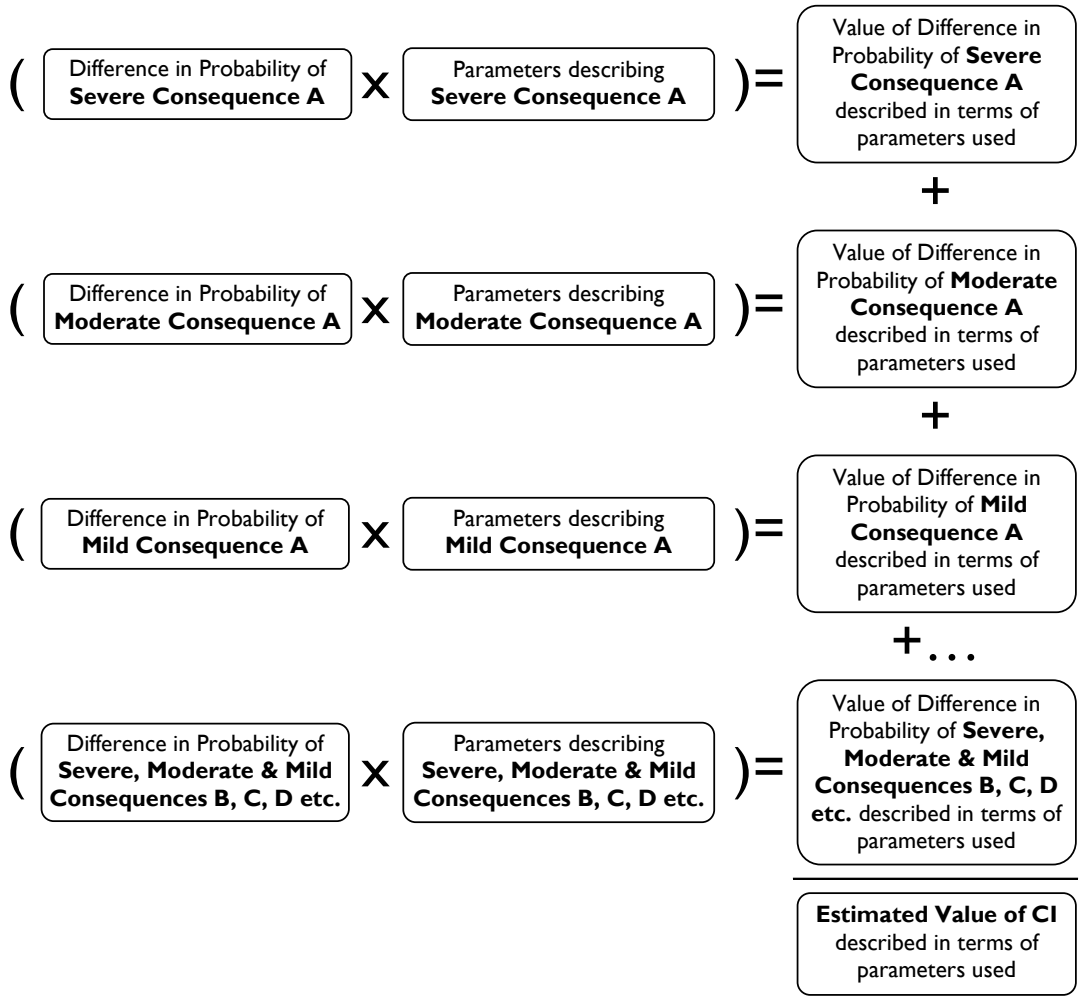

FIGURE 8 - CALCULATION OF VALUE OF INTERVENTION FROM EXPERT OPINION. "CI" INDICATES CLINICAL INTERVENTION. REPRODUCED FROM STAFFORD *ET AL*.[191]

Having established the overall value of an intervention, the final component of Tenni's methodology attempts to account for the fact that pharmacists are not the only party able to identify and resolve DRPs.

Attribution

In many situations, a DRP addressed by the pharmacist may be identified and resolved by another person (Figure 6, Scenario 2). Tenni identified that past studies evaluating pharmacists' interventions falsely assumed that no other health professional would have intervened, had the pharmacist not performed the intervention.[204] By not

considering the likelihood of another party identifying the intervention, the value attributed to the pharmacist was overestimated. Tenni (as described by Stafford *et al*.[191]) asserted that for an appropriate proportion of the value of the intervention to be assigned to the pharmacist's activity, some estimate of this likelihood (termed *attribution*) was necessary. To estimate the value of the pharmacist's involvement in resolving a DRP using this methodology, the attribution value is multiplied by the total value of the intervention.

The concept of attribution raises major challenges regarding assignment of appropriate values. It is likely that the attribution for each intervention would be different depending upon the circumstances of the intervention. Hence, individual interventions must be assigned an attribution value in some way. It is not possible to use literature values to assign attribution as there are no studies to date that have compared the likelihood of non-pharmacists to pharmacists in undertaking medication-related interventions in primary care. Therefore, to overcome this issue, Stafford *et al*. contested that the opinion of experienced clinicians derived via a consensus method was the most appropriate source for assigning valid attributions to each intervention.[191] They recommended obtaining attribution levels for an intervention by asking experts to answer the following question for each intervention they assess:

> *"Based on your experience, what is the likelihood of someone other than the patient's community pharmacist performing this intervention?"*

Furthermore, by obtaining multiple opinions of attribution for the same intervention, this approach facilitates uncertainty analysis (discussed in section 2.4.4 below).

2.4.2.2.3 Drug costs

The perspective of the cost-analysis was from that of the Australian government, so only PBS-listed items were included in the medication cost analysis. All items were costed on the basis of quantity of drug used per month. Medications for which the quantity required for a one month supply was different to the PBS maximum quantity were costed by calculating the fraction of the PBS maximum quantity used each month and multiplied by the dispensed price. As documentation regarding the frequency of

most medications taken on a when-required basis was generally poor, these medications were not included in the drug cost analysis as this was likely to introduce an unacceptable level of uncertainty into the measurement of drug costs. In calculating the changes in drug costs resulting from the HMRs, it was assumed that any changes to the patients' medication regimens would be sustained for 12 months following the HMR.

2.4.2.3 Valuation of resources

2.4.2.3.1 HMR

The cost of each HMR was $323.80 which included both payment to the accredited pharmacy ($183.60) and GP (MBS item 900, value $140.20)[xii].

2.4.2.3.2 Health resources

In Australia, extensive data regarding the duration and cost of hospitalisation are available for most conditions, grouped according to Australian Refined Diagnosis Related Groups (AR-DRGs).[208] The cost and median length of hospital admission (ALOS) was derived from 2006-7 AR-DRGs version 5.1 values for public hospitals Australia-wide. Further detail regarding hospitalisation costs is provided in Chapter Three of this thesis. Previous studies of HMRs have costed outpatient medical services according to MBS codes,[86, 139, 144] which are costs of the services that are billed to the Medicare program and therefore the Australian government.[209] based on this precedence, outpatient medical services were costed using the appropriate MBS codes as at November 2008. At this time, the cost used for a GP consultation (MBS item 23) was $33.55. Pathology items were costed according to the appropriate MBS item number. The cost used for an initial specialist visit (MBS item 104) was $79.05. For subsequent specialist visits, the cost used was $39.70 (MBS item 105).

[xii] reimbursement levels as at November 2008

2.4.2.3.3 Drug costs

Calculating the change in medication costs was performed by costing the changes to each patient's medication regimen that occurred as a result of the HMR. Medications subsidised by the PBS were costed using the dispensed price for the maximum quantity in the November 2008 Schedule of Pharmaceutical Benefits issued by the Australian Government Department of Health and Ageing.[210] It was assumed that all patients were Commonwealth concession card holders; hence, each item attracted a patient co-payment of $5.00 (current at the time of the study).

2.4.3 Time horizon

A time horizon for both costs and cost savings of 12 months was assumed. This was to reflect the intention that the patient management plan is to be reviewed by the GP and pharmacist at 12-monthly intervals, and patients are eligible for a HMR annually. Furthermore, it is likely that extending the time horizon beyond 12 months would increase the uncertainty in the experts' predictions. It should be acknowledged that some authors have suggested that the outcomes resulting from MMRs may not become apparent for at least 12 months,[66, 114] therefore the estimate generated by this study should be considered conservative.

2.4.4 Sensitivity and uncertainty analysis

A number of key assumptions were made in determining the value of the HMRs in this study using this methodology:

- that the basis for determining the value of the consequences is a reasonable estimate of both the health resource utilisation and quality of life effects incurred by each consequence;
- that each experts' selection of consequences and assignment of pre- and post-HMR probabilities to them are appropriate and reasonable estimates;
- that the assignment of attribution values by the experts are plausible estimates;
- that the uptake values obtained from the outcomes data are appropriate and accurate;

- that the extrapolation of the assessed HMRs to the whole sample is appropriate; and
- that the sample of HMRs in the VALMER study is representative of HMRs nation-wide.

Several of these assumptions were investigated using sensitivity analysis as there is inherent uncertainty in several of the assumptions made and parameters estimated using the methodology described. Sensitivity analyses explore the extent to which the conclusions derived from a study are dependent upon underlying assumptions or data that are subject to measurement errors.[211] Scenario analysis is a type of sensitivity analysis that involves a series of scenarios that typically include a baseline case (the "best guess"), the most optimistic (the "best case") and the most pessimistic (the "worst case").[212] A scenario analysis was therefore undertaken by modifying the following variables:

1. varying the HMR cost, as this component contributed the most to the overall difference in costs between the with- and without HMR states. Firstly, the cost was increased by 10% to estimate the effect of omitting rural loading allowances from the baseline scenario. Second, the cost was decreased to the amount paid only to the pharmacy (that is, no reimbursement to the GP) to investigate the cost-effectiveness of the pharmacy component of the HMR.
2. removal of the attribution component from the model; that is, assigning 100% of the potential benefits and detriments resulting from the HMRs to the medication review. As neither of the two previous Australian studies that utilised expert opinion to estimate the outcomes of HMRs involved an attribution component,[86, 139] this scenario is closest to them in methodological terms.
3. varying the proportion of the pharmacists' recommendations that were implemented following the HMR. In the baseline scenario, the HMRs without outcomes were discounted by the overall proportion of implemented recommendations to account for the probability that they may not have been implemented (81.8%, Section 5.4.6.1). Furthermore, in this scenario, the recommendations not implemented were valued at zero. Hence, the outcomes data essentially discounted the costs and QOL effects associated with

recommendations that were not enacted following the HMR. In the first alternate scenario, it was assumed that all recommendations made by the pharmacists to resolve the DRPs were implemented by the GP. By not discounting these recommendations, this scenario investigated the *potential* value of the HMRs, rather than the *realised* value as calculated in the baseline scenario. It also provided a proxy indication of the appropriateness (as considered by the experts) of the recommendations made in the HMR. Intuitively, when compared to the baseline scenario estimates, decreased costs or improved QOL in this scenario would suggest that the recommendations that were not enacted would have resulted in benefits if they had been enacted. In the second scenario, the lowest rate of implemented recommendations reported in previous studies of HMRs (42%)[126] was used to discount the recommendations with unknown outcomes to estimate the "worst case".

4. inclusion of DRPs not assessed by the experts. In the baseline scenario, only the first three DRPs identified in the HMR reports were assessed by the experts (discussed in detail in Section 2.6.1). However, based on previous studies of HMRs (Table 2), it was anticipated that the number of DRPs documented in many of the HMR reports would be greater than this. By evaluating only the first three DRPs in the HMRs, a substantial number of the DRPs in the baseline scenario would be valued at zero. To investigate the costs and QOL effects of these DRPs on the HMRs, each DRP not included in the expert assessment was valued at the average value of the DRPs assessed by the experts to estimate the "best case". In consideration that these DRPs may have been of lower clinical significance (and therefore less valuable) than the first three DRPs addressed in the HMRs, the average DRP value was discounted by 25%, 50% and 75%, respectively. In each of these scenarios, drug costs were calculated as per the baseline scenario.

The variables modified in the sensitivity analysis are shown in Table 23.

TABLE 23 - VARIABLES MODIFIED IN SCENARIO ANALYSES

VARIABLE	BASELINE SCENARIO	ALTERNATE SCENARIO/S
HMR cost	• $323.80	• $356.18 (+10% assumed for rural loading - "worst case") • $183.60 (pharmacist payment only)
Attribution to pharmacist	• Expert assigned	• 100% (attributes all benefit to HMR)
Inclusion of DRPs not valued by experts	• Omitted from analysis	• Each DRP not assessed by experts valued at average value of DRP, discounted by 0%, 25%, 50% and 75% ("best case")
Uptake of recommendations	• Outcomes data (average for missing values)	• Missing valued assigned a probability of uptake of 42% (minimum value from literature - "worst case")

2.4.5 Cost-utility analysis

The summary statistic calculated was the incremental cost-effectiveness ratio (ICER, or cost per QALY gained). The mean ICER does not yield any information as to the degree of uncertainty of the estimate. To derive an estimate of the uncertainty, the data were re-sampled 5000 times using a nonparametric bootstrap approach to generate a mean cost and QALY gain from the HMRs and the resulting ICERs were calculated. Bootstrapping involves large numbers of repetitive computations to estimate the shape of a variable's distribution.[213] By using bootstrapping, the uncertainty around the mean ICER may be represented by a cost-effectiveness acceptability curve (CEAC), which is interpreted as the probability that the ICER is below a threshold of acceptance.

As per the WHO-CHOICE definitions of cost-effectiveness,[185] thresholds of $50 000 and $150 000 per QALY were used to provide an indication of the cost-effectiveness of HMRs.

2.5 Sample size

As discussed previously, by using expert opinion to estimate health resource utilisation instead of measuring the actual usage resulted in a smaller sample size requirement. The sample size was therefore arbitrarily calculated but limited by the

funding grant which provisioned for data regarding up to 1000 HMRs to be collected, with the experts assessing a sample of 180 of the HMRs.

The study design involved 16 "medication therapy experts" who were allocated to one of four panels. Each panel assessed 90 HMRs, sixty of which were common to all four panels, and thirty that were unique to each panel. Hence sixteen expert opinions were provided for sixty HMRs and four opinions for 120 HMRs, resulting in a total of 180 HMRs undergoing expert assessment. This approach was used by Buurma and Tenni to maximise the number of interventions that were assessed by the experts,[193, 204] and is illustrated in Figure 9.

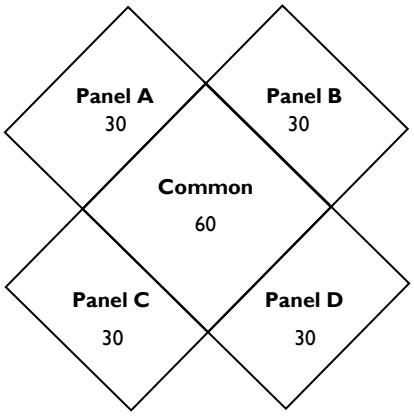

FIGURE 9 - DESIGN OF PANELS FOR HMR ASSESSMENT BY EXPERTS

2.6 Expert assessment of HMRs

2.6.1 Assessment of DRPs

Whilst the method described by Tenni and Stafford *et al*. involved interventions undertaken in community pharmacies, it was thought reasonable to assume that it may be adapted to undertake evaluations of HMRs in this study. As discussed previously, HMRs are concerned with preventing or resolving DRPs, and the types of DRP identified in HMRs appears to be influential in their cost-effectiveness. Hence, to investigate avenues for improving the cost-effectiveness of HMRs, it was considered appropriate for the expert panels to assess the individual DRPs addressed in the HMRs, rather than the entire HMR. It was assumed that the net effect of each HMR was the sum of the consequences resulting from each of the DRPs addressed in the HMR.

Anecdotal evidence from previous research suggested that Tenni's method is time-consuming and somewhat fatiguing for the experts performing the assessment. It was anticipated that the first DRPs addressed in the HMRs would be the most clinically relevant, and potentially the most valuable (Section 2.1.3.1). Whilst it was desirable for each expert to evaluate every DRP in the HMRs, this approach was considered to be impractical. Consequently, the experts evaluated the first three DRPs documented in each HMR, and these results were then extrapolated to the remainder of the DRPs in the sensitivity analysis (Section 2.4.4).

2.6.2 Selection of experts

There are no strict criteria governing the selection of experts for participation in clinical panels. With regard to medical research, Jones and Hunter defined the term "expert" to be "*clinicians practicing in the field under consideration*".[214] According to this definition, suitable experts for this study included pharmacists and medical practitioners. It has been recommended that experts should be selected based on their appropriateness for the study in terms of experience, reputation, geographic representation, practice type and specialty, and heterogeneity in treatment patterns.[206] Wright *et al.* demonstrated that community pharmacists, hospital pharmacists, GPs and hospital physicians attribute significantly different values when undertaking these assessments.[143] They concluded that all four types of practitioners should be included in clinical panels.

Based on these recommendations, a panel of specialist and general medical practitioners, and hospital and community pharmacists was recruited. With regard to the type of specialist medical practitioners, it was assumed that a broad, practical knowledge of general medicine would be required; hence, general physicians and clinical pharmacologists were invited to participate. This was done via emailed requests for expressions of interest distributed by the Internal Medicine Society of Australian and New Zealand (IMSANZ) and the Australasian Society of Clinical and Experimental Pharmacologists and Toxicologists (ASCEPT) (Appendix IX).

Two GPs expressed interest in the study having seen the promotional materials seeking HMR submissions from pharmacists. These GPs were invited to participate in

the clinical panel assessment, and one of these GPs recruited a further two GP colleagues for the desired number of GPs.

2.6.3 Collection of individual opinions

An online system was built to collect the experts' assessments of the HMRs. Each expert was provided with an individualised logon; upon logging on to the system they selected a case to review. At this point they were presented with a copy of the case details, including the patient's demographics, medical conditions and medications. The DRPs identified in the HMR report were also displayed on this screen.

An example is shown in Figure 10.

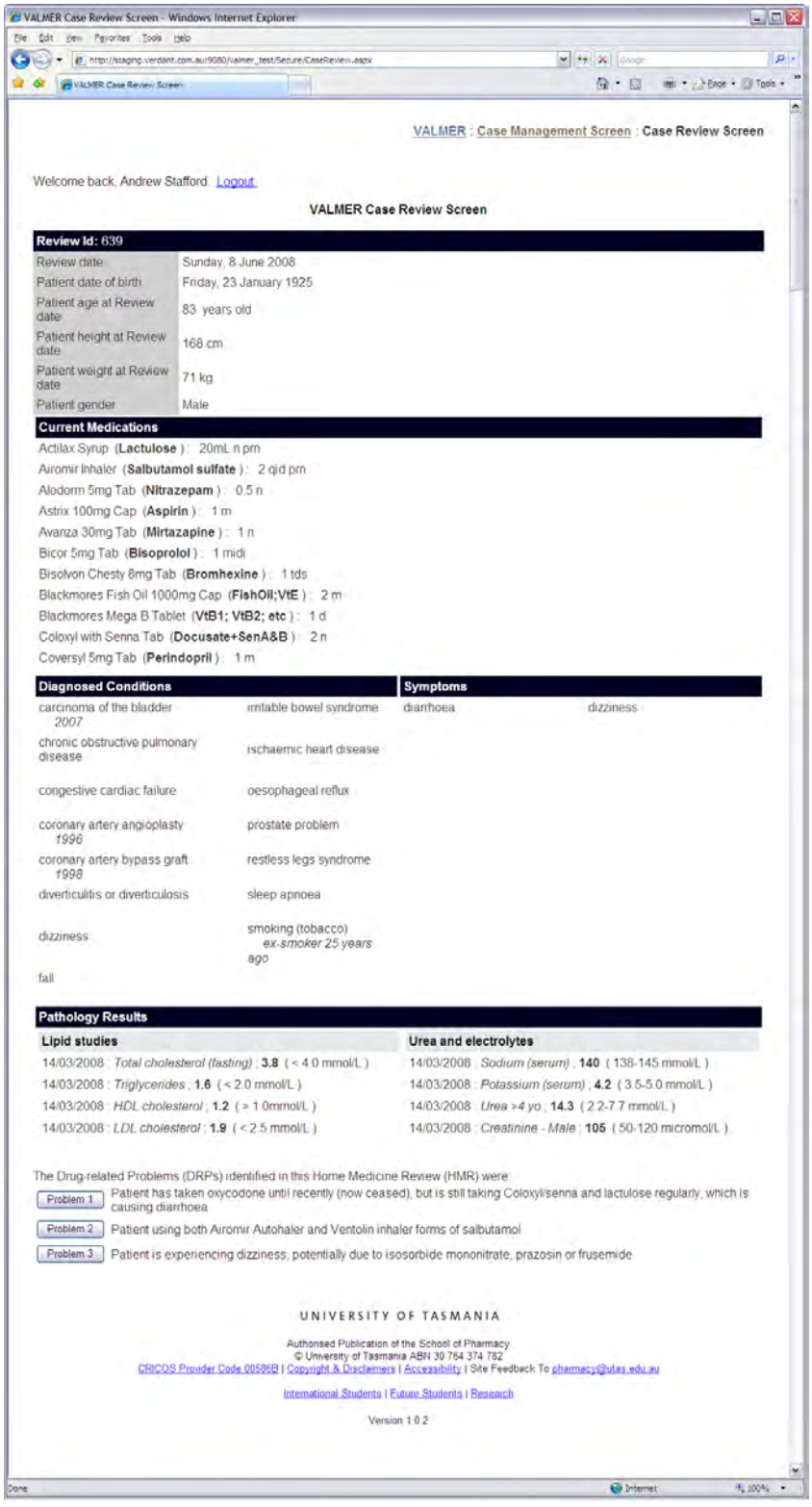

FIGURE 10 - SCREENSHOT OF CASE SUMMARY SCREEN IN EXPERT ASSESSMENT SYSTEM

The expert was then taken to another screen where they selected the consequences and entered their predictions for the outcomes of the recommendations made by the pharmacist to resolve or prevent each DRP. The expert's estimate of the attribution to the HMR for each DRP was also entered at this stage (Figure 11).

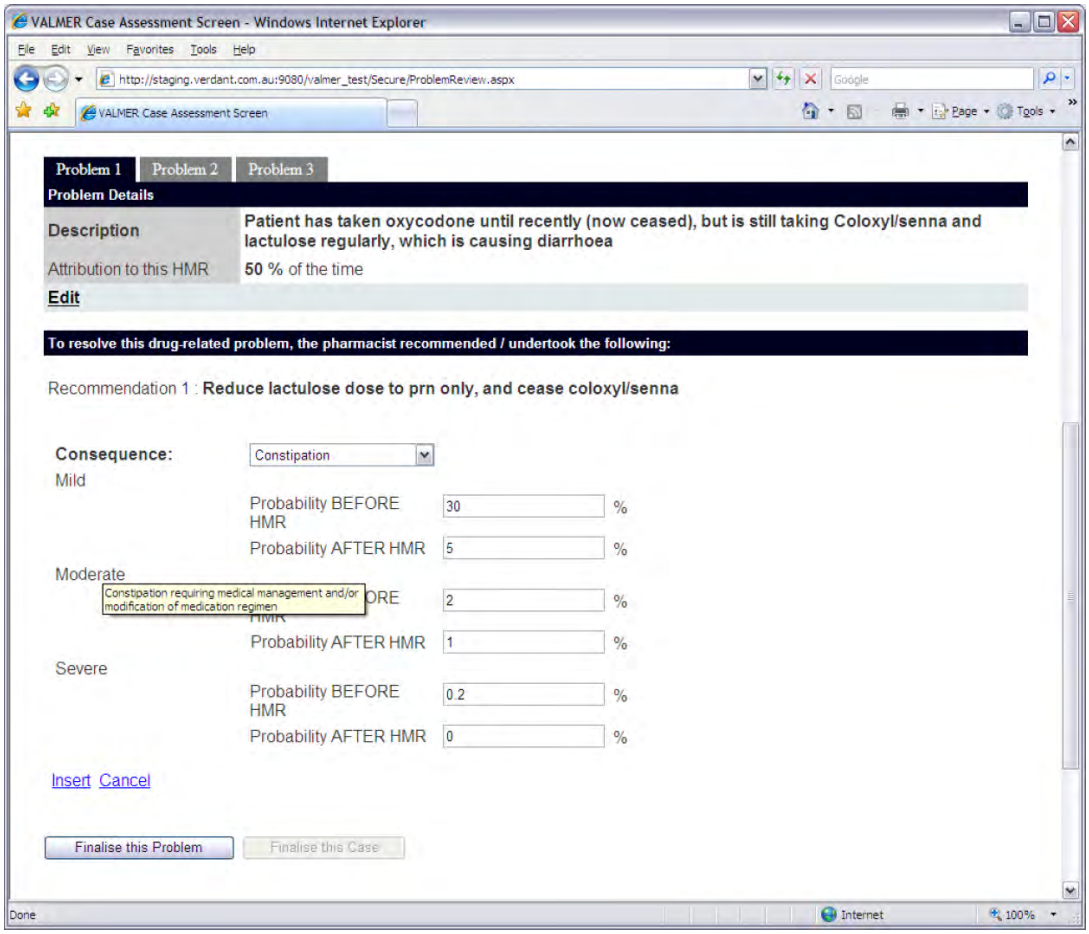

FIGURE 11 - SELECTION OF CONSEQUENCES AND ENTRY OF THEIR BEFORE- AND AFTER-HMR PROBABILITIES BY EXPERTS

Recruitment for the panels of experts commenced in February 2009, and the assessment was conducted between March and July 2009. Each expert was provided with a training manual (Appendix XI) and given the opportunity to discuss the assessment process with a member of the research team at the commencement of their assessments.

2.6.4 Consensus of opinion

Once the experts had assessed every HMR, it was then necessary to aggregate their individual opinions. Two general approaches that have been used to elicit opinions from experts were considered, namely formal consensus methods (*behavioural aggregation*) and individual elicitation (*mathematical aggregation*).[215] Consensus methods involve approaches such as the Delphi and Nominal Group techniques whereby several rounds of opinion-gathering and review are employed to reach a consensus of opinion regarding the intervention under consideration.[216] Conversely, individual elicitation involves asking a panel of experts to independently judge the probability of an event occurring, and then aggregating their opinions using approaches such as linear pooling and random effects meta-analysis.[215] Whilst not explicitly stated, it is apparent that the prior studies of HMRs that utilised expert opinion to generate cost-effectiveness estimates used some form of consensus methodology to do so,[139, 144] and not individual elicitation.

However, a relatively recent review concluded there are no clear benefits of forced consensus methods over individual elicitation methods with mathematical aggregation.[141] Furthermore, Philips *et al*. asserted that variability in expert opinion should be incorporated into economic models, and consensus of opinion should not be forced.[217] In consideration of this, each expert was asked to predict the outcomes of each HMR in isolation (that is, no formal consensus methodology was applied).

The initial plan was to aggregate the probability estimates for each consequence selected by the experts to generate an overall estimate of the likelihood of each consequence occurring before and after the intervention. The software program @RISK (Palisade Corporation, Ithaca, NY) contains a module that identifies the statistical distribution function that best fits a data set.[218] To do so, the software uses the following step-wise approach:

1. For each distribution type, estimates of the parameters that describe the distribution are generated using maximum-likelihood estimators;
2. The fit for each distribution is optimised using the Levenberg-Marquardt method;[219, 220]

3. The goodness-of-fit for the optimised function is measured using chi-square goodness of fit, Kolmogorov-Smirnov and/or Anderson-Darling tests;
4. The goodness-of-fit statistics for each distribution are then compared, and the distribution with the best fit is used.[218]

However, once the data was collected, it was apparent that distribution fitting would not be possible for many of the parameters due to substantial variation between the experts with regards to both their probability estimates and the consequences they selected (discussed in detail in Section 6.3.3.2 page 298). Rather than make assumptions regarding the distributions of these parameters, simple averages for the probability estimates of each consequence were used. It should be recognised that this is a significant limitation to the representation of the uncertainty intervals of the ICERs generated in the study. To partially account for this issue, another scenario analysis was undertaken whereby the analysis was performed using the average of each expert's estimates with *No consequence* responses removed.

2.7 Statistical analysis

Data was stored in an Access 2007 (Microsoft Corporation, Redmond, WA, USA) database specifically created for the study. Most tables and graphs were developed using Excel 2010 (Microsoft Corporation, Redmond, WA, USA). Probabilistic sensitivity analysis (PSA) was performed using @RISK for Excel Version 5.5 (Palisade Corporation, Ithaca, NY, USA). This software was also used to develop cost-effectiveness acceptance curves and scatter plots for resampled data.

All statistical analysis was undertaken using PASW Statistics Version 19 (IBM Corporation, Somers, NY, USA). Data that was parametrically distributed was analysed as follows:

- means of different groups were compared using Students' *t*-tests; and
- means for repeated measures were compared using paired *t*-tests.

Data that was non-parametrically distributed was analysed as follows:

- medians of different groups were compared using Mann-Whitney U-tests;

- medians for repeated measures were compared using Wilcoxon signed ranks tests;
- χ^2 tests for independence were used to compare proportions between groups; and
- χ^2 tests for goodness of fit were used to compare proportions in samples with those of known populations.

Unless indicated otherwise, for all analyses a *P* value of 0.05 was used as the threshold for statistical significance. For certain post-hoc comparisons, Bonferroni adjustment was applied to the alpha level (P=0.05) for judging statistical significance to maintain the alpha across all tests at a reasonable level.[221] Bonferroni adjustment is achieved by dividing the alpha level by the number of comparisons.

Reliability was investigated using Cronbach's α and Fleiss' κ. Correlation between variables was investigated using Pearson product-moment correlation coefficient and Kendall's non-parametric test.

Chapter 3 - Costing health resource utilisation

3.1 Introduction

The following two chapters provide an overview of the Consequences table developed by Tenni and address several methodological limitations inherent in the technique.[204] In Chapter 4, a development of the methodology is presented, whereby the technique may be used to provide an indication of the QOL effects resulting from pharmacists' interventions, in addition to healthcare costs.

3.1.1 Creation of the list of consequences

The list of potential consequences was developed in a two-stage process. The list was initially formulated by Tenni based on experience and knowledge of the consequences commonly affected by community pharmacist interventions. Each severity level of each consequence (that is, each health state) was described by a vignette predominantly based on literature definitions whenever possible. For example, the vignettes for the consequence of "bleeding" were based on definitions used by Crowther *et al*. and Schulman et al.,[222, 223] and are shown in Table 24.

TABLE 24 - VIGNETTES FOR EXAMPLE CONSEQUENCE OF "BLEEDING". ADAPTED FROM TENNI [204]

SEVERITY LEVEL (HEALTH STATE)	DESCRIPTION
Mild	Easy bruising, bleeding from small cuts, petechia, ecchymosis, mild elevation of INR not requiring adjustment of dosage
Moderate	Haematoma, epistaxis, blood loss from mouth, vagina, melena, eye bleed, haematuria, haematemesis, moderate elevation of INR requiring modification of dose of anticoagulant
Severe	Severe bleeding requiring hospitalisation, blood product and/or haemodynamic support

Tenni initially used this list in a pilot study where a panel of 16 experts (4 community pharmacists, 4 hospital pharmacists, 6 GPs and 2 specialist physicians) identified any additional consequences they considered necessary to estimate the outcomes of community pharmacy CIs.[204] Descriptive vignettes were then assigned to these new consequences using the same process as for the initial list. Each consequence was also

grouped according to its corresponding AR-DRG Major Diagnostic Criteria (MDC) to assist with classification. The final list of the 51 consequences is shown in Table 25 grouped according to their MDC categories.

TABLE 25 - CONSEQUENCES DESCRIBED IN TENNI'S CONSEQUENCES TABLE

Diseases & Disorders of Blood, Blood Forming Organs, Immunological Disorders • Anaemia • Bone marrow suppression	**Diseases & Disorders of the Eye** • Glaucoma
Diseases & Disorders of the Circulatory System • Arrhythmia • Heart Failure • Hypertension • Hypotension • Myocardial Ischaemia	**Diseases & Disorders of the Digestive System** • Constipation • Diarrhoea • Gastrointestinal pain • Liver Disease • Nausea • Gastrointestinal bleeding
Diseases & Disorders of the Kidney & Urinary Tract • Urinary Incontinence • Urinary retention • Urinary Tract Infection • Renal Dysfunction • Serotonin toxicity	**Diseases & Disorders of the Respiratory System** • Asthma • Chronic Airways Disease • Respiratory depression
Injuries, Poisonings & Toxic Effects of Drugs • Allergic reaction	**Mental Diseases & Disorders** • Anxiety • Depression • Insomnia • Psychosis
Diseases & Disorders of the Musculoskeletal System & Connective Tissue • Myopathy • Osteoporosis	**Diseases & Disorders of the Skin, Subcutaneous Tissue & Breast** • Rash
Endocrine, Nutritional & Metabolic Diseases & Disorders • Acidosis • Alkalosis • Hypoglycaemia • Hypocalcaemia • Hypokalaemia • Hypothyroidism	• Diabetes • Hypercalcaemia • Hyperkalaemia • Hyperthyroidism

Diseases & Disorders of the Nervous System		**Various**	
• Cerebrovascular event	• Confusion	• Bleeding, non-specific	• CNS Depression
• Dementia	• Headache	• Pain	• Oedema
• Parkinsonism	• Seizures	• Infection, general	

3.1.2 Parameters describing each consequence

A crucial element of the methodology involved the assignment of values to consequences for the health resources utilised and disability incurred (that is, QOL) when the consequences occurred. The parameters assigned to Tenni's consequences table are shown in Table 26.[xiii]

TABLE 26 - PARAMETERS ASSIGNED TO CONSEQUENCES. MODIFIED FROM TENNI[204]

DURATION AND SEVERITY	
• Level of impact on health (QOL)	• Total duration of illness
HEALTH RESOURCE UTILISATION	
• Hospitalisation duration and cost	• Number and cost of specialist consultations
• Number and cost of GP consultations	• Laboratory and pathology investigations

The values assigned to each of these parameters were obtained from a combination of literature sources and expert opinion. Costing schedules (such as the Australian MBS and PBS) were available for the health resource utilisation parameters. However, for each parameter except hospitalisation, what was unknown was the number of times each of these resources would be utilised every time a consequence occurs. Tenni did not extensively document the methodology employed to address this issue;[204] however, it seems that a two-stage process was used to generate point estimates for each of these parameters. Initial estimates for these parameters were made by Tenni, which were then reviewed and modified by an informal consensus group process that included a physician, a GP and two pharmacists.

An example of the values assigned to the consequence of "Seizures" in Tenni's consequences table is shown in Table 27. Three shortcomings are noteworthy:

xiii Given the similar role of pharmacists in both HMRs and community pharmacy interventions, it is unsurprising that the health resources costed in Tenni's consequences table were aligned with the costs to be considered in the VALMER study. As discussed in section 2.4.2.1 of this thesis, the costs to be considered in the VALMER study (excluding drug and HMR service costs) were hospitalisations, GP visits, specialist visits and laboratory tests/ investigations.

- only point estimates of each parameter are provided, without acknowledgement of the considerable degree of uncertainty of each estimate;
- there is no quantification of the impact of each health state on QOL; only the generic descriptions of *Mild*, *Moderate* and *Severe*; and
- the costings are reasonably outdated.

TABLE 27 - VALUES ASSIGNED CONSEQUENCE OF "SEIZURES" IN TENNI'S CONSEQUENCES TABLE. REPRODUCED FROM [204]

SEVERITY CODE (HEALTH STATE)	HEALTH STATE DESCRIPTION	LEVEL OF HEALTH STATUS IMPACT	DURATION OF ILL HEALTH (DAYS)	DURATION (COST) OF HOSPITAL ADMISSION (DAYS)*	NUMBER (COST†) OF GP CONSULTS
MILD	Mild one-off seizure unlikely to recur or require management	1	7	0.00 ($0)	2 ($56)
MODERATE	Requiring medical attention or modification of medication regimen	2	60	0.00 ($0)	4 ($112)
SEVERE	Severe seizures requiring hospitalisation and intravenous anticonvulsants	3	90	2.05 ($1,606)	2 ($56)

SEVERITY CODE (HEALTH STATE)	NUMBER (COST†) OF SPECIALIST CONSULTS	INVESTIGATIONS OR OTHER COST†	TOTAL DIRECT COSTS	ADMISSION COST AND DURATION SOURCE *	INVESTIGATION OR OTHER COST NOTES
MILD	0 ($0)	$104	$160		EEG
MODERATE	0 ($0)	$122	$234		EEG, Bloods
SEVERE	2 ($192)	$0	$1,854	B76B	

* National Hospital Cost Data Collection Cost Weights for ARE-DRG Version 4.2, Round 7 (2002-2003)
† 2005 Medicare Benefits Schedule

Tenni's complete consequences table is presented in Appendix XII.

The general aim of the projects discussed in the following two chapters was to address these limitations. To do so, two projects were undertaken, with the following overarching objectives:

- to update the costs assigned to the health states;
- to improve the quantification of the impact of each health state on QOL; and

- to appropriately account for the uncertainty of these estimates.

For simplicity, these were broadly broken down into costs associated with hospitalisation and non-hospitalisation treatments. This chapter is concerned with updating the estimated costs of the health states, and appropriately account for their uncertainty.

3.2 Methods

3.2.1 Hospitalisation

Extensive Australian data regarding the duration and cost of hospitalisation is available for most admissions through the Australian Hospital Statistics.[208] These are grouped according to AR-DRGs. For consequences associated with several DRGs, the number of separations[xiv] was used as a proxy indicator for the probability of each DRG occurring. To calculate the mean cost and ALOS, a relative weighting of each DRG according to proportion of separations was initially calculated. This weighting was then multiplied by the mean cost and ALOS for each DRG, and the summation of these values was used as the mean cost and ALOS for each health state.

The following worked example illustrates the process used to calculate the hospitalisation costs used in the study. The health state of *Severe cerebrovascular event* is described as *"CVA resulting in severe symptoms and signs requiring hospitalisation and medical management (e.g. stroke)"*. There are four DRGs relating to hospital admissions due to stroke. These, the number of separations, their ALOS and cost per separation are shown in Table 28.

[xiv] As defined by the Australian Hospital Statistics: *Separation is the term used to refer to the episode of admitted patient care, which can be a total hospital stay (from admission to discharge, transfer or death) or a portion of a hospital stay beginning or ending in a change of type of care (for example, from acute care to rehabilitation). Separation also means the process by which an admitted patient completes an episode of care by being discharged, dying, being transferred to another hospital or by a change of care type.*[208]

TABLE 28 - DRG DATA FOR "CEREBROVASCULAR EVENT" [208]

DRG	DESCRIPTION	NUMBER OF SEPARATIONS	ALOS (DAYS)	MEAN COST PER SEPARATION
B70A	Stroke with catastrophic complication or comorbidity	6 504	17	$15 233
B70B	Stroke with severe complication or comorbidity	7 194	9.6	$8 487
B70C	Stroke without catastrophic or severe complication or comorbidity	7 155	6.3	$5 533
B70D	Stroke, died or transferred within five days	6 230	1.5	$2 292

To calculate the probability of each DRG contributing to a hospitalisation resulting from the consequence, the ALOS and mean cost per separation were multiplied by the percentage of total number of separations linked to the consequence (Table 29).

TABLE 29 - CALCULATION OF ALOS AND HOSPITALISATION COSTS FOR "SEVERE CEREBROVASCULAR EVENT" FROM DRG DATA

DRG	NUMBER OF SEPARATIONS	FRACTION OF SEPARATIONS	ALOS (DAYS) X FRACTION OF SEPARATIONS	MEAN COST PER SEPARATION X FRACTION OF SEPARATIONS
B70A	6 504	0.2	4.1	$3 658.20
B70B	7 194	0.3	2.6	$2 254.40
B70C	7 155	0.3	1.7	$1 461.80
B70D	6 230	0.2	0.3	$527.20
TOTAL	**27 083**	**1.0**	**8.6**	**$7 901.59**

Using this methodology, each health state resulting in hospitalisation was costed and the length of stay determined using the most up to date Australian Hospitalisation Statistics available at the time (2006-2007).[208]

3.2.2 Non-hospitalisation treatment

3.2.2.1 Overview

Datasets equivalent to the Australian Hospital Statistics are not readily available for patients managed outside of hospital. An Australian database collects data regarding

GP encounters (Bettering the Evaluation And Care of Health (BEACH) project).[224] However, the cost of accessing this data was very high (several thousands of dollars per health state). As the table of standard consequences described 153 health states (51 consequences, each at three levels of severity), it was concluded that using the BEACH database was prohibitively expensive.

In the absence of empirical data, expert opinion was employed to generate an estimate of the utilisation of these remaining health resources, and the duration of each health state. It was considered that GPs were the most appropriate experts to employ for this aspect of the study as the majority of the parameters to be estimated related to primary care encounters.

A panel of GPs was recruited via advertisements placed in a widely distributed electronic newsletter in June 2009 (Appendix XII). No formal selection criteria were applied, and whilst there was no target sample size, the study budget permitted for a maximum of 20 GPs to participate. To assess their interests and workplace experience, each GP also completed a short questionnaire (Appendix XIV).

Prior to commencing the study, each participating GP was provided with a study overview and instruction manual (Appendix XV). Using three internet-based questionnaires, they each provided point estimates of the number of GP and specialist visits required to resolve each health state. They also estimated the pathology/laboratory investigations that would be ordered as part of the management for each health state, and provided an estimate of the duration of each health state (termed *days of ill health*).

An example questionnaire is shown in Figure 12.

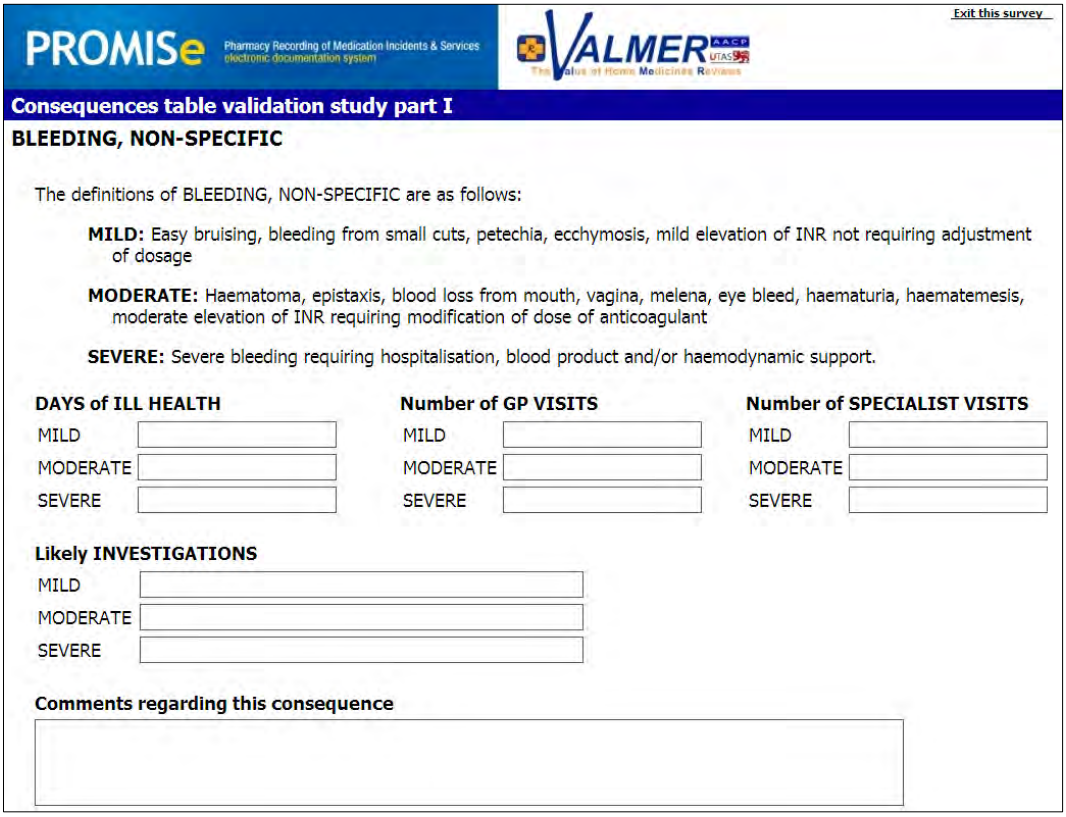

FIGURE 12 - EXAMPLE OF ONLINE QUESTIONNAIRE USED BY GPS TO ASSIGN HEALTH-RESOURCE UTILISATION TO CONSEQUENCES

Once the number of GP and specialist visits, and number and type of laboratory investigations were estimated, costing each health state was straightforward using the Australian Government Medicare Benefits Costs Schedule November 2008.[225]

3.2.3 Analysis

3.2.3.1 Aggregation of opinions

To represent the experts' individual estimates for each parameter as a single overall estimate, mathematical aggregation was employed by using PSA to represent the uncertainty between each expert's estimates for each parameter (described in Section 2.6.4). Exact estimates were unrealistic, as the consequences table is designed to describe an aggregate of the management of a group of patients with similar characteristics (comparable to a case mix group, akin to DRG data).[204]

In order for PSA to be robust, the distributions which are defined must be appropriate. The specific parameters of the distribution were determined using the best-fit function included in @RISK 5.5 (Palisade Corporation, Ithaca, NY, USA), described in Section 2.6.4. This program attempts to find the best parameters for a distribution around a given set of raw data.[218] The advantage of using a best-fit approach around the raw data produced by the experts is that it helps to ensure that the resultant distribution is appropriately representative of the data collected.[226] Further to this, if many uncertain variables are present in the economic model, it is a relatively simple task to automate the distribution fitting process.

In consideration of this, every expert's response for each resource in each health state were considered to be valid and included into distribution fitting using @RISK 5.5. A macro was written for Excel 2007 (Microsoft Corporation, Redmond WA, USA) to assess each of the sets of expert opinions and attempt to fit a best-fit probabilistic distribution to the set of values they had indicated in their assessments using @RISK 5.5's best-fit algorithm. Depending upon the particular variable, the macro performed the following:

- For the continuous variable (duration of illness), the best-fit algorithm was restricted to using only the @RISK BetaGeneral distribution as the expert assessments had a limited bound between 0 and 365 days.[227] In cases where the algorithm could not find a fit due to a degenerate distribution, the fall-back of a calculated Beta distribution was used, based on the standard α_1 and α_2 parameters. In the event that a Beta distribution could not be calculated, a simple, fixed mean of the expert values was used.

- For discrete variables (number of GP and specialist visits), the best-fit discrete distribution was used. χ^2 values for binomial, geometric, negative binomial and Poisson distributions were calculated,[227] and the distribution with the best χ^2 was used. For consequences where a distribution was not found due to all assessors agreeing, a fixed average value was used.

For the laboratory and pathology investigations, PSA and distribution fitting was not possible as each expert selected different tests. Consequently, each expert's responses were coded according to the appropriate MBS item/s numbers. For each health state, the number experts who indicated that a test would be performed was divided by the total number of experts to act as a proxy indicator for the probability that the particular test would be ordered. For each test that at least one expert indicated would be ordered for a health state, the probability of the test occurring was multiplied by the MBS cost, then summed to calculate the total cost of the laboratory investigations to be ordered for that health state.

3.2.3.2 Validity

With regard to assessing the validity of the results, in the absence of testing against empirical data there are no exact criteria to validate them. However, it is likely that a desirable criterion for the results to be considered reliable would be for mutual coherence; that is, the costs and duration of illness for the health states of any given consequence should be ordered *Mild* < *Moderate* < *Severe*. As these types of data tend to be non-parametric,[228] the median of these estimates was used for this analysis. As shown in the results, the data were found to be primarily non-parametric in nature, justifying this approach.

To further assess the validity of the results, it was assumed that the duration of a health state would be related to the costs associated with resolving it; that is, positive correlation existed between duration of illness and the costs of healthcare. Whilst this analysis would not identify results that were unrealistic or non-sensible, it would provide a general indication as to the validity of the data as a whole. Based on this assumption, the correlation between the duration of illness and total costs of health states was tested. The validity of this assumption was investigated using the only

empirical data available which was the hospitalisation statistics: positive correlation between the length of stay and cost would suggest some validity of the results.

An additional investigation into the validity of the results was undertaken by comparing the values derived in this study to those developed by Tenni in the original study.

3.3 Results

3.3.1 Duration and cost of hospitalisation

Of the 153 health states described in the consequences table, 44 were described as requiring hospitalisation to manage. Three of these health states were of *moderate* severity level (*cerebrovascular event*, *gastrointestinal bleeding* and *myocardial ischaemia*), with the remainder being *severe*. The median number of DRGs mapped to each health state was 3, ranging from 1 (for example, *Headache* and *Allergic reaction*) to 78 (*Infection*). Health states affecting psychological conditions that required comparatively long durations of admission, such as *Psychosis* and *Depression*, resulted in high costs. Cardiovascular health states involving thromboembolic events were also costly to resolve. Conversely, health states requiring shorter durations of admission were generally less costly to resolve.

To investigate whether the assumptions regarding the planned correlation analysis was valid, the relationship between the length of stay and cost was investigated using Pearson product-moment correlation coefficient and Kendall's non-parametric test. As expected, both tests of correlation indicated that there was a strong correlation between the length of stay and admission costs ($r=0.69$, $n=51$, $P<0.001$, tau-b value=0.57, $P<0.001$).

This relationship is illustrated in Figure 13.

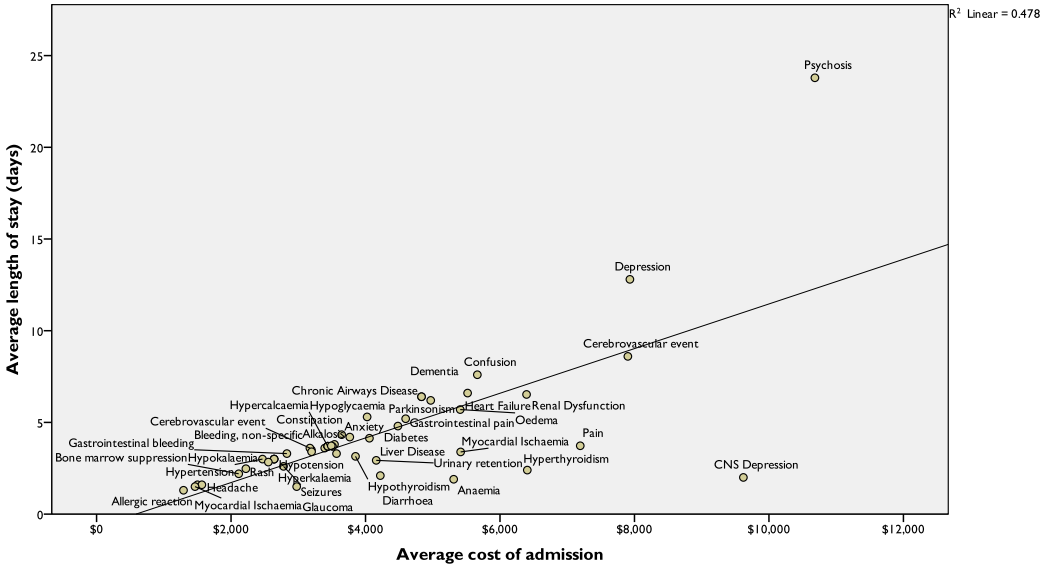

FIGURE 13 - SCATTERPLOT ILLUSTRATING THE RELATIONSHIP BETWEEN LENGTH OF STAY AND HOSPITALISATION COSTS

A complete list of the hospitalisation data assigned to the health states is presented in the completed consequences table (Appendix XVII Table 148).

3.3.2 Duration of illness and cost of non-hospitalisation treatment

The expert assessment process used to value the non-hospitalisation treatment for each health state was conducted during a six-week period that commenced in late June 2009. During this time, 19 GPs expressed an interest in participating in the study, and 14 GPs completed it. Reasons for non-participation included lack of time and loss of interest by the GP. For the GPs who completed the study, the mean time to perform the assessment was 210 minutes (SD 128 minutes, range 64 to 501 minutes).

3.3.2.1 Characteristics of the experts

Seven of the 14 GPs indicated their state of primary practice was Victoria, whilst the remainder practiced in New South Wales (3, 21%), Queensland (2, 14%), the Australian Capital Territory and Western Australia (1 from each, 7%). With regard to the age of their "typical" patient, all but three responded that they saw adults aged between 18 and 65 years. Two of the remaining GPs primarily saw "older adults"

(aged over 65 years), whilst the final GP saw an even mix from infants through to the frail elderly. Consequently, every GP described the living situation of their "typical" patients as "*Living at home without carer assistance*".

Half of the GPs saw more female patients than male, whilst all but one of the remainder (who saw more male than female patients) saw an even number of males and female patients. With regards to their areas of special interest, the most frequently identified fields were dermatology, paediatrics and sexual health (Table 30).

TABLE 30 - AREAS OF SPECIAL INTEREST FOR GP PANEL MEMBERS

AREA OF SPECIALITY INTEREST	NUMBER (%) OF RESPONDENTS
Andrology	2 (14%)
Cardiology	5 (36%)
Dermatology	6 (43%)
Endocrinology	5 (36%)
Gastroenterology	4 (29%)
Geriatrics	4 (29%)
Gerontology	2 (14%)
Gynaecology/obstetrics	5 (36%)
Infectious diseases	4 (29%)
Ophthalmology	2 (14%)
Palliative medicine	3 (21%)
Paediatrics	6 (43%)
Psychiatry	4 (29%)
Radiology	2 (14%)
Rheumatology	2 (14%)
Sexual health	6 (43%)
Sports medicine	4 (29%)

In general, the majority of the assessors completed the study with little difficulty. However, three of the 14 GPs did not provide details of the laboratory tests they would order as part of the management of each health state; instead, they only counted how many tests they would order. Consequently, 11 opinions were obtained for pathology and laboratory tests.

3.3.2.2 Duration of illness

The experts' predictions of the duration of illness for each consequence are shown in Table 31. In general, as the severity level of a consequence increased from *Mild* through *Moderate* to *Severe*, the duration also increased. It is interesting that for many *Mild* health states, at least one expert indicated that any ill health was unlikely to be experienced by a patient. As the severity level of the consequences increased, there were fewer health states that were considered to incur no symptomatic ill health. Consequently, the median duration of each consequence increased as the severity increased from *Mild* to *Moderate* then *Severe*. Overall, the median estimated duration of ill health increased from 2 days for the *Mild* health states, to 7 days for the *Moderate* and 17 days for the *Severe* health states.

TABLE 31 - EXPERT ESTIMATES OF DAYS OF ILL HEALTH OF CONSEQUENCES AT DIFFERENT SEVERITY LEVELS

CONSEQUENCE	DAYS OF ILL HEALTH								
	SEVERITY	MILD			MODERATE			SEVERE	
	STATISTICS	MEAN ± ST DEV	MEDIAN [IQR]	RANGE	MEAN ± ST DEV	MEDIAN [IQR]	RANGE	MEAN ± ST DEV	MEDIAN [IQR]	RANGE
Acidosis		8.9 ± 26.3	2 [2]	0 to 100	11.4 ± 12.6	8.5 [9]	1 to 50	22.5 ± 17.1	22.5 [23]	1 to 60
Alkalosis		9.4 ± 26.2	1.5 [4]	0 to 100	8.5 ± 15.1	3 [4]	2 to 60	17.6 ± 16.3	10 [14]	5 to 50
Allergic reaction		1.5 ± 1.3	1 [3]	0 to 3	3.8 ± 2.8	3 [3]	0 to 10	8.4 ± 5.6	7 [10]	1 to 20
Anaemia		13.4 ± 21.5	2.5 [14]	0 to 60	18.8 ± 18.2	12 [25]	0 to 60	32.2 ± 27.7	20 [15]	7 to 90
Anxiety		15.8 ± 24.5	6 [13]	0 to 80	37.1 ± 52.2	10 [45]	3 to 180	77.9 ± 97.2	22 [126]	7 to 300
Arrhythmia		8.1 ± 10.3	4 [4]	1 to 40	21.6 ± 29.9	10 [23]	4 to 120	40.1 ± 58.6	25.5 [15]	7 to 240
Asthma		6.9 ± 7.2	4 [8]	0 to 20	13.6 ± 12.3	7 [15]	3 to 40	37.1 ± 46.0	14.5 [40]	7 to 180
Bleeding, non-specific		3.1 ± 5.1	2 [2]	0 to 20	7.6 ± 7.8	5 [4]	2 to 30	22.1 ± 22.2	14 [20]	1 to 90
Bone marrow suppression		6.6 ± 8.9	3 [6]	0 to 30	18.1 ± 26.4	7 [5]	0 to 90	51.0 ± 68.6	27 [26]	5 to 250
Cerebrovascular event		3.9 ± 2.7	3 [3]	1 to 10	10.1 ± 7.3	8.5 [9]	2 to 30	106.2 ± 132.1	60 [80]	1 to 365
Chronic Airways Disease		9.3 ± 10.5	4 [7]	0 to 30	19.8 ± 22.8	12 [13]	5 to 90	59.8 ± 98.2	30 [44.5]	4 to 365
CNS Depression		8.2 ± 10.6	3 [8]	0 to 30	29.1 ± 37.6	14 [25]	2 to 120	83.2 ± 133.9	27.5 [61]	3 to 365
Confusion		5.2 ± 5.2	4 [5]	0 to 20	17.8 ± 23.1	10 [15]	2 to 90	62.5 ± 106.4	25 [25.5]	1 to 365
Constipation		6.1 ± 10.7	2.5 [7]	0 to 40	11.7 ± 16.2	6 [12]	0 to 60	22.6 ± 22.4	12 [26]	2 to 70
Dementia		61.6 ± 107.4	10.5 [88.5]	0 to 365	143.5 ± 176.0	30 [358]	7 to 365	217.0 ± 176.3	365 [335]	14 to 365
Depression		9.2 ± 10.6	4 [7]	0 to 30	24.1 ± 24.9	14 [33]	4 to 90	79.6 ± 96.3	55 [71]	14 to 365
Diabetes		5.8 ± 5.7	3 [4]	0 to 20	10.8 ± 7.5	7 [8]	4 to 30	41.5 ± 67.1	20 [16]	7 to 250
Diarrhoea		2.9 ± 2.7	2 [4]	0 to 10	8.2 ± 6.4	7 [7]	1 to 20	15.0 ± 12.4	10 [14]	1 to 40
Gastrointestinal bleeding		1.9 ± 2.1	1 [3]	0 to 7	8.8 ± 7.8	7 [5]	2 to 30	31.7 ± 49.9	14 [13]	3 to 180
Gastrointestinal pain		9.9 ± 26.0	2.5 [3]	0 to 100	11.2 ± 9.7	8.5 [10]	2 to 40	27.6 ± 36.8	14.5 [20]	1 to 144
Glaucoma		5.5 ± 8.7	2 [3]	0 to 28	24.8 ± 51.9	5 [26]	3 to 200	45.5 ± 97.4	15 [23]	2 to 365
Headache		4.9 ± 10.4	1 [5]	0 to 40	8.4 ± 9.0	4.5 [11]	0 to 30	17.2 ± 17.7	10 [17]	3 to 60

Consequence	Days of ill health								
	Severity	Mild			Moderate			Severe	
	Statistics	Mean ± st dev	Median [IQR]	Range	Mean ± st dev	Median [IQR]	Range	Mean ± st dev	Median [IQR]	Range
Heart Failure		33.1 ± 95.8	5 [12]	0 to 365	49.4 ± 94.2	20 [33]	3 to 365	112.6 ± 134.6	45 [185]	7 to 365
Hypercalcaemia		4.0 ± 5.7	2 [3]	0 to 21	10.6 ± 10.0	5 [15]	2 to 30	26.4 ± 30.9	14.5 [20]	2 to 120
Hyperkalaemia		2.7 ± 5.6	1 [2]	0 to 21	7.9 ± 9.5	4.5 [2]	3 to 30	18.9 ± 21.8	12 [10]	3 to 90
Hypertension		1.9 ± 5.3	0 [1]	0 to 20	6.5 ± 13.1	2.5 [5]	0 to 50	32.8 ± 51.1	14 [23]	0 to 180
Hyperthyroidism		5.1 ± 5.2	4.5 [6]	0 to 20	12.5 ± 10.0	8.5 [16]	2 to 30	32.4 ± 27.8	25 [30]	4 to 90
Hypocalcaemia		3.7 ± 5.2	2 [4]	0 to 20	9.4 ± 9.5	5 [6]	2 to 30	24.5 ± 37.7	10.5 [18]	4 to 150
Hypoglycaemia		3.8 ± 5.9	1.5 [2]	0 to 20	8.1 ± 9.5	3.5 [4]	2 to 30	14.4 ± 13.7	7 [15]	1 to 45
Hypokalaemia		3.6 ± 5.0	1.5 [2]	0 to 14	10.3 ± 15.8	4.5 [7]	1 to 60	27.4 ± 45.4	12 [23]	3 to 180
Hypotension		4.1 ± 6.9	1.5 [5]	0 to 25	9.9 ± 9.8	6 [7]	2 to 30	21.2 ± 23.5	10 [23]	2 to 90
Hypothyroidism		8.8 ± 12.1	2.5 [14]	0 to 30	14.7 ± 17.0	8.5 [17]	0 to 60	27.1 ± 32.0	12.5 [42]	4 to 120
Infection, general		3.1 ± 3.0	2 [7]	0 to 7	9.9 ± 7.5	7 [9]	2 to 28	22.6 ± 16.5	17 [20]	5 to 60
Insomnia		8.3 ± 12.7	2 [9]	0 to 40	16.6 ± 20.5	6 [16]	2 to 60	29.0 ± 29.1	14 [53]	3 to 90
Liver Disease		4.4 ± 8.5	0.5 [3]	0 to 30	12.7 ± 14.1	5 [16]	0 to 40	48.2 ± 61.5	21.5 [50]	3 to 180
Myocardial Ischaemia		6.1 ± 7.9	3 [5]	1 to 30	13.1 ± 13.6	8.5 [11]	2 to 45	40.3 ± 47.4	30 [10]	1 to 180
Myopathy		9.1 ± 16.3	2 [7]	0 to 50	13.0 ± 15.7	4.5 [12]	1 to 50	18.3 ± 15.8	10 [23]	4 to 50
Nausea		3.2 ± 3.8	2 [2]	0 to 14	6.4 ± 6.4	4 [4]	2 to 21	13.1 ± 13.5	7 [10]	1 to 45
Oedema		4.0 ± 7.9	1 [5]	0 to 30	9.8 ± 11.5	5.5 [7]	2 to 40	37.9 ± 65.3	17 [24]	4 to 250
Osteoporosis		28.0 ± 97.0	1.5 [4]	0 to 365	47.3 ± 94.5	14 [33]	3 to 365	84.6 ± 102.0	30 [62]	5 to 365
Pain		6.8 ± 10.2	2.5 [6]	0 to 30	13.9 ± 12.9	10 [13]	2 to 50	71.7 ± 106.4	22 [85]	7 to 365
Parkinsonism		38.1 ± 97.5	7 [8]	0 to 365	83.2 ± 127.5	30 [40]	7 to 365	200.8 ± 162.6	200 [320]	14 to 365
Psychosis		8.5 ± 9.8	4.5 [7]	0 to 30	43.4 ± 77.7	17 [23]	4 to 300	91.7 ± 101.5	60 [70]	7 to 365
Rash		3.1 ± 3.9	2 [3]	0 to 14	11.9 ± 15.3	6 [10]	1 to 60	48.2 ± 92.6	17.5 [30]	7 to 365
Renal Dysfunction		1.4 ± 1.9	1 [2]	0 to 7	7.2 ± 4.5	6 [4]	4 to 21	41.6 ± 75.4	25.5 [20]	2 to 300
Respiratory depression		3.4 ± 3.7	2 [4]	0 to 14	11.9 ± 9.5	8.5 [15]	3 to 30	48.7 ± 76.2	25 [32]	7 to 300

CONSEQUENCE	DAYS OF ILL HEALTH								
	SEVERITY	MILD			MODERATE			SEVERE		
	STATISTICS	MEAN ± ST DEV	MEDIAN [IQR]	RANGE	MEAN ± ST DEV	MEDIAN [IQR]	RANGE	MEAN ± ST DEV	MEDIAN [IQR]	RANGE
Seizures		2.4 ± 1.5	2 [2]	0 to 5	6.0 ± 3.8	5 [2]	2 to 18	29.2 ± 32.9	20 [20]	1 to 100
Serotonin toxicity		3.7 ± 5.5	2 [4]	0 to 21	9.4 ± 8.6	7 [6]	3 to 35	15.2 ± 11.9	12 [13]	3 to 45
Urinary Incontinence		5.4 ± 8.9	2 [5]	0 to 30	31.1 ± 53.9	10 [16]	2 to 200	100.6 ± 133.3	30 [64]	7 to 365
Urinary retention		3.6 ± 5.5	2 [3]	0 to 21	7.9 ± 8.2	5 [3]	1 to 30	21.9 ± 25.4	10 [23]	1 to 90
Urinary Tract Infection		1.9 ± 1.6	1 [2]	0 to 5	3.9 ± 1.5	4 [2]	1 to 7	11.5 ± 6.1	10 [8]	1 to 21

As was expected, there was substantial variation between the experts with regard to their predicted duration of illness for each health state. Boxplots illustrating the difference between the experts are shown in Figure 14, Figure 15 and Figure 16.

For the *Mild* health states (Figure 14), experts 5, 7 and 13 rated several consequences as incurring longer durations of ill health than the remaining experts. Interestingly, these consequences were generally chronic, incurable conditions (for example, heart failure, dementia and Parkinsonism), which may partially account for the long duration of illness.

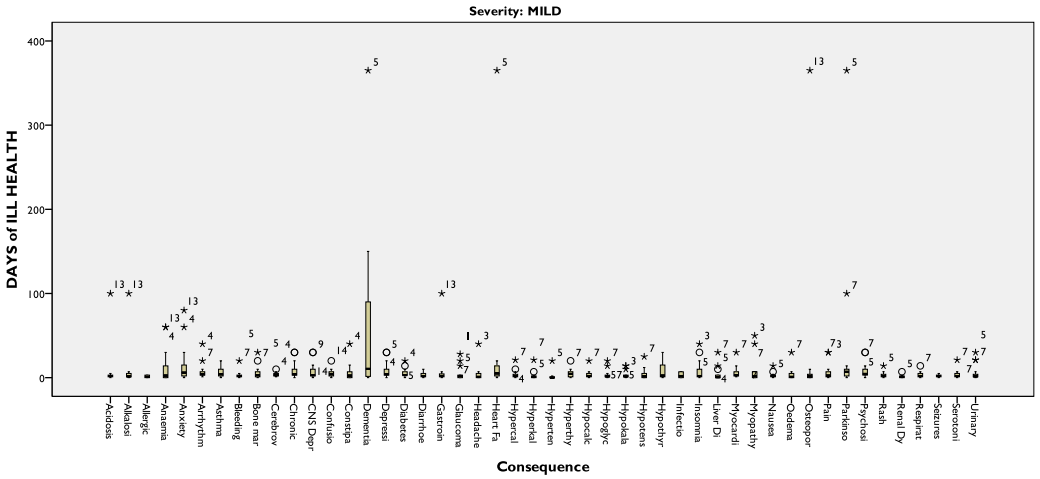

FIGURE 14 - DIFFERENCES BETWEEN EXPERTS' OPINIONS OF LIKELY DURATION OF CONSEQUENCES AT *MILD* SEVERITY LEVEL. NUMBERS DENOTE RESPONSES OF INDIVIDUAL EXPERTS.

Further differences between the experts' opinions were evident in the duration of the *Moderate* health states (Figure 15). However, in contrast to the *Mild* states, there were no experts whose opinions were consistently discordant to the others. Again, the consequences with the greatest variation between the experts included *Heart failure*, *Dementia* and *Parkinsonism*.

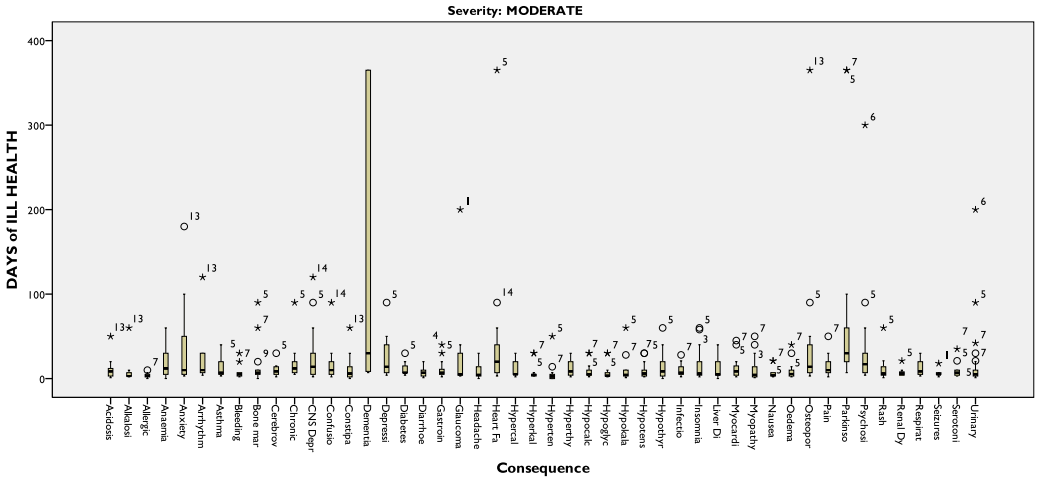

FIGURE 15 - DIFFERENCES BETWEEN EXPERTS' OPINIONS OF LIKELY DURATION OF CONSEQUENCES AT *MODERATE* SEVERITY LEVEL. NUMBERS DENOTE RESPONSES OF INDIVIDUAL EXPERTS.

For the *Severe* health states, the discordance between the experts was marked (Figure 16). Interestingly, the median duration for the consequence of *Dementia* was 365 days, which is perhaps indicative of the lack of effective treatment for this condition.

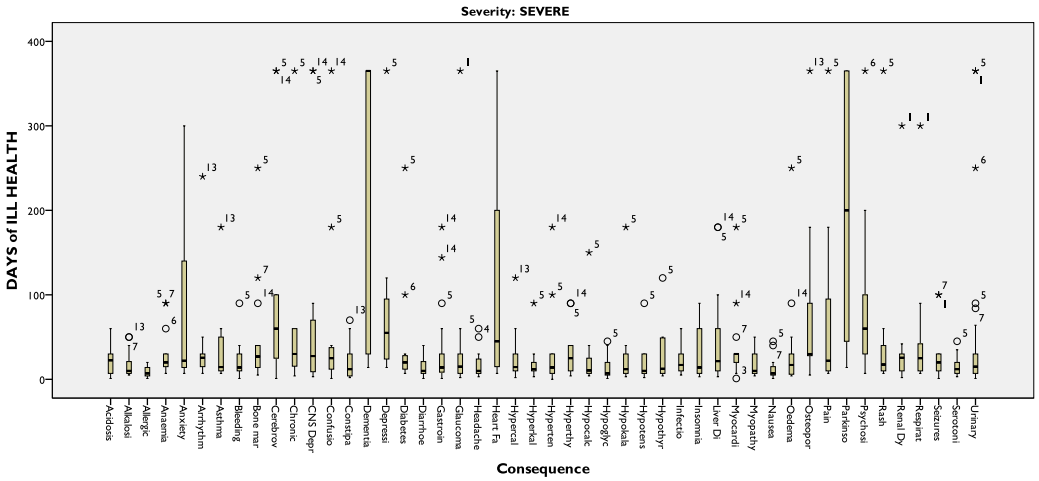

FIGURE 16 - DIFFERENCES BETWEEN EXPERTS' OPINIONS OF LIKELY DURATION OF CONSEQUENCES AT *SEVERE* SEVERITY LEVEL. NUMBERS DENOTE RESPONSES OF INDIVIDUAL EXPERTS.

3.3.2.3 GP visits

Summary statistics of the experts' predictions of the number of GP visits required to resolve each health state are shown in Table 32. Considerable variation between the experts' opinions for many of the consequences is evident, and, as with their predictions of the number of days of ill health, the discordance between them generally increased with the severity of the consequences, potentially due to the generally greater number of GP visits occurring with the more severe health states. Despite the variation between the experts, for every consequence the median number of GP visits increased with the severity of the consequence.

TABLE 32 - EXPERT ESTIMATES OF GP VISITS REQUIRED TO RESOLVE CONSEQUENCES AT DIFFERENT SEVERITY LEVELS

CONSEQUENCE	NUMBER OF GP VISITS								
	SEVERITY	MILD			MODERATE			SEVERE	
	STATISTICS	MEAN ± ST DEV	MEDIAN [IQR]	RANGE	MEAN ± ST DEV	MEDIAN [IQR]	RANGE	MEAN ± ST DEV	MEDIAN [IQR]	RANGE
Acidosis		1.8 ± 1.5	2 [1]	0 to 6	5.0 ± 5.7	4 [2]	1 to 24	6.0 ± 5.0	5 [8]	1 to 15
Alkalosis		2.5 ± 3.0	1.5 [1]	1 to 12	3.6 ± 2.1	3 [2]	2 to 10	6.0 ± 5.0	5 [3]	1 to 20
Allergic reaction		1.5 ± 1.3	1 [0]	0 to 5	2.4 ± 1.5	2 [0]	1 to 6	5.0 ± 5.0	3 [2]	1 to 20
Anaemia		2.4 ± 2.0	2 [2]	0 to 7	3.9 ± 1.8	3.5 [2]	1 to 8	7.0 ± 5.0	5 [4]	1 to 20
Anxiety		3.0 ± 3.0	2 [1]	0 to 12	5.4 ± 2.1	4.5 [3]	3 to 10	9.0 ± 4.0	9 [4]	4 to 20
Arrhythmia		2.7 ± 1.9	2 [2]	1 to 7	5.1 ± 2.9	4 [3]	2 to 13	7.0 ± 4.0	7 [3]	1 to 20
Asthma		1.6 ± 1.0	1.5 [1]	0 to 4	3.4 ± 1.5	3 [3]	1 to 6	5.0 ± 3.0	5 [2]	1 to 12
Bleeding, non-specific		2.0 ± 1.4	1 [2]	1 to 5	3.6 ± 2.0	3 [2]	2 to 8	5.0 ± 5.0	4 [3]	1 to 18
Bone marrow suppression		2.6 ± 1.4	2.5 [1]	1 to 6	4.4 ± 1.7	4 [2]	3 to 9	6.0 ± 4.0	6 [4]	1 to 15
Cerebrovascular event		3.4 ± 1.5	3.5 [2]	1 to 6	5.1 ± 2.5	4.5 [2]	2 to 10	8.0 ± 7.0	7 [6]	1 to 30
Chronic Airways Disease		3.2 ± 2.2	3 [3]	1 to 8	5.1 ± 3.6	4 [2]	1 to 15	7.0 ± 6.0	7 [4]	1 to 25
CNS Depression		2.2 ± 1.2	2 [2]	1 to 5	5.0 ± 2.7	4.5 [2]	2 to 12	8.0 ± 5.0	7 [6]	1 to 18
Confusion		2.1 ± 1.0	2 [1]	1 to 4	4.1 ± 1.7	3.5 [1]	2 to 8	6.0 ± 3.0	5 [4]	2 to 15
Constipation		1.1 ± 1.2	1 [1]	0 to 4	2.9 ± 2.2	2 [1]	1 to 10	4.0 ± 2.0	4 [2]	1 to 10
Dementia		3.2 ± 1.7	3 [3]	1 to 6	5.6 ± 3.2	5 [4]	2 to 12	9.0 ± 6.0	7 [6]	2 to 20
Depression		3.2 ± 2.8	2 [1]	1 to 10	5.9 ± 4.5	5 [3]	2 to 20	8.0 ± 7.0	6 [5]	1 to 30
Diabetes		2.8 ± 1.8	3 [3]	0 to 6	4.7 ± 2.3	4.5 [3]	2 to 10	7.0 ± 5.0	6 [4]	1 to 20
Diarrhoea		1.0 ± 0.7	1 [0]	0 to 3	2.1 ± 0.8	2 [0]	1 to 4	4.0 ± 2.0	3 [2]	1 to 8
Gastrointestinal bleeding		2.0 ± 1.0	2 [2]	1 to 4	3.4 ± 1.5	3.5 [2]	1 to 6	5.0 ± 3.0	4 [3]	1 to 10
Gastrointestinal pain		1.1 ± 1.2	1 [0]	0 to 5	2.6 ± 1.2	3 [1]	1 to 5	5.0 ± 3.0	4 [3]	1 to 12
Glaucoma		1.7 ± 1.0	2 [1]	0 to 4	3.1 ± 1.5	3 [2]	1 to 6	5.0 ± 2.0	5 [3]	1 to 10
Headache		0.8 ± 1.6	0 [1]	0 to 6	1.8 ± 1.0	2 [1]	0 to 4	3.0 ± 2.0	3 [2]	1 to 10

Consequence	Number of GP visits								
	Severity	Mild			Moderate			Severe	
	Statistics	Mean ± st dev	Median [IQR]	Range	Mean ± st dev	Median [IQR]	Range	Mean ± st dev	Median [IQR]	Range
Heart Failure		3.0 ± 2.0	2.5 [2]	0 to 7	6.4 ± 4.0	5 [4]	1 to 15	9.0 ± 6.0	9 [8]	1 to 20
Hypercalcaemia		1.6 ± 1.2	1.5 [1]	0 to 5	3.4 ± 1.4	3.5 [2]	1 to 6	5.0 ± 3.0	5 [3]	1 to 15
Hyperkalaemia		1.6 ± 0.9	2 [1]	0 to 3	3.6 ± 1.6	3.5 [3]	1 to 6	7.0 ± 8.0	5 [3]	2 to 30
Hypertension		2.1 ± 1.5	2 [2]	0 to 5	4.6 ± 2.7	4 [5]	0 to 8	8.0 ± 7.0	7 [6]	1 to 30
Hyperthyroidism		2.1 ± 2.0	1.5 [2]	0 to 8	3.9 ± 1.9	3.5 [2]	1 to 8	5.0 ± 4.0	4 [2]	0 to 15
Hypocalcaemia		1.7 ± 1.0	2 [1]	0 to 3	3.9 ± 1.6	4 [2]	1 to 7	5.0 ± 3.0	5 [3]	1 to 15
Hypoglycaemia		1.6 ± 1.2	2 [1]	0 to 4	3.6 ± 1.8	3 [2]	1 to 8	6.0 ± 3.0	6 [3]	1 to 15
Hypokalaemia		1.6 ± 0.6	2 [1]	0 to 2	3.5 ± 1.7	4 [2]	1 to 7	5.0 ± 3.0	6 [3]	1 to 15
Hypotension		1.5 ± 1.0	2 [1]	0 to 3	3.8 ± 1.8	3.5 [1]	1 to 8	6.0 ± 4.0	6 [4]	1 to 15
Hypothyroidism		2.3 ± 1.7	2 [2]	0 to 7	4.0 ± 1.6	4 [1]	2 to 8	5.0 ± 3.0	5 [2]	1 to 12
Infection, general		1.3 ± 1.3	1 [1]	0 to 5	2.7 ± 1.0	2.5 [2]	1 to 4	4.0 ± 3.0	4 [2]	1 to 12
Insomnia		0.9 ± 0.9	1 [1]	0 to 3	2.6 ± 1.1	2.5 [2]	1 to 4	5.0 ± 3.0	4 [2]	2 to 12
Liver Disease		1.4 ± 1.2	1.5 [2]	0 to 3	4.1 ± 1.5	4 [2]	1 to 6	6.0 ± 4.0	6 [4]	1 to 20
Myocardial Ischaemia		2.4 ± 1.5	2 [3]	0 to 5	4.4 ± 2.1	4 [3]	1 to 8	6.0 ± 3.0	6 [4]	1 to 15
Myopathy		1.3 ± 1.2	1 [2]	0 to 4	2.8 ± 1.0	3 [1]	1 to 5	5.0 ± 1.0	5 [2]	2 to 7
Nausea		0.9 ± 0.6	1 [0]	0 to 2	2.4 ± 1.1	2 [1]	1 to 4	3.0 ± 1.0	3 [2]	1 to 6
Oedema		0.9 ± 0.6	1 [0]	0 to 2	2.9 ± 1.2	3 [2]	1 to 5	5.0 ± 3.0	5 [3]	1 to 12
Osteoporosis		2.1 ± 1.3	2 [1]	0 to 4	4.6 ± 2.6	4 [2]	0 to 10	6.0 ± 4.0	5 [2]	1 to 15
Pain		1.4 ± 1.2	1 [2]	0 to 3	3.5 ± 1.5	3.5 [2]	2 to 6	7.0 ± 4.0	6 [4]	1 to 15
Parkinsonism		2.8 ± 1.8	2.5 [2]	0 to 6	5.3 ± 3.1	4 [2]	2 to 12	8.0 ± 5.0	8 [4]	2 to 20
Psychosis		2.1 ± 1.0	2 [2]	1 to 4	5.0 ± 2.6	4 [2]	2 to 12	6.0 ± 4.0	6 [4]	1 to 15
Rash		0.6 ± 0.6	0.5 [1]	0 to 2	2.5 ± 1.3	2.5 [2]	0 to 4	4.0 ± 2.0	4 [1]	1 to 10
Renal Dysfunction		1.6 ± 1.3	2 [2]	0 to 4	3.9 ± 1.7	4 [3]	1 to 6	6.0 ± 3.0	6 [4]	1 to 12
Respiratory depression		1.2 ± 0.9	1.5 [2]	0 to 2	3.6 ± 1.7	3 [3]	1 to 6	5.0 ± 3.0	5 [2]	1 to 12

Consequence	Number of GP visits								
	Severity	Mild			Moderate			Severe		
	Statistics	Mean ± st dev	Median [IQR]	Range	Mean ± st dev	Median [IQR]	Range	Mean ± st dev	Median [IQR]	Range
Seizures		2.0 ± 1.4	2 [1]	1 to 6	4.1 ± 2.1	3.5 [3]	2 to 8	5.0 ± 4.0	5 [3]	1 to 15
Serotonin toxicity		1.3 ± 0.7	1 [1]	0 to 2	3.6 ± 2.2	3 [1]	1 to 10	5.0 ± 3.0	4 [2]	2 to 14
Urinary Incontinence		0.9 ± 0.8	1 [1]	0 to 2	3.2 ± 1.3	3 [2]	2 to 6	5.0 ± 3.0	4 [2]	1 to 10
Urinary retention		1.1 ± 0.8	1 [1]	0 to 2	2.6 ± 0.9	2.5 [1]	1 to 4	4.0 ± 2.0	4 [1]	1 to 8
Urinary Tract Infection		0.6 ± 0.5	1 [1]	0 to 1	1.4 ± 0.5	1 [1]	1 to 2	3.0 ± 1.0	3 [1]	0 to 6

At the *Mild* severity level, many of the experts considered that a GP visit would not be required to resolve the consequence (Figure 17). The health state with the greatest discordance of opinion was that of *Allergic reaction*, where seven of the 14 experts estimated that one GP visit would be required to resolve the consequence, and the estimates by the remaining GPs ranged from 0 to 12 visits.

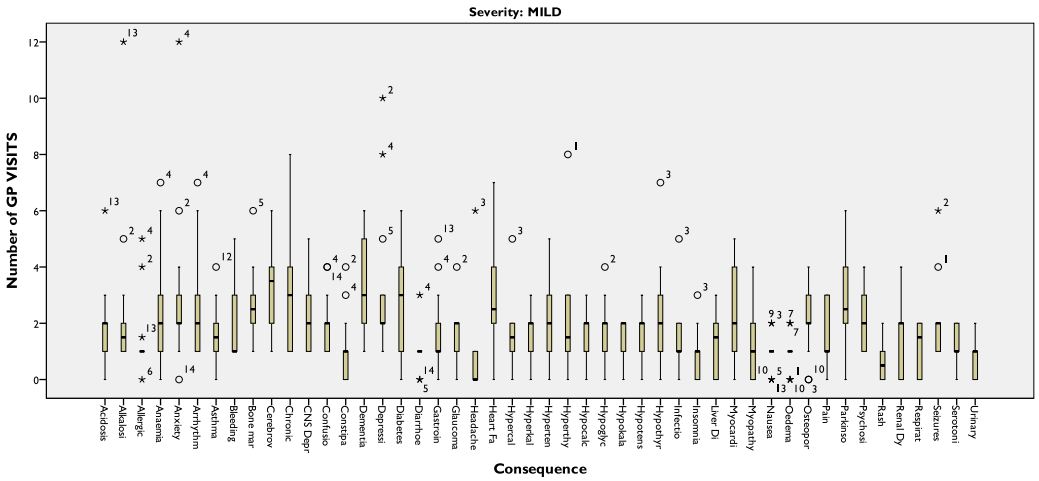

FIGURE 17 - DIFFERENCES BETWEEN EXPERTS' OPINIONS REGARDING THE NUMBER OF GP VISITS REQUIRED TO RESOLVE CONSEQUENCES AT *MILD* SEVERITY LEVEL. NUMBERS DENOTE RESPONSES OF INDIVIDUAL EXPERTS.

The variation between the experts' predictions regarding the number of GP visits required to resolve the *Moderate* health states is shown in Figure 18. It is evident that Expert 2 predicted a greater number of GP visits would be required to resolve many of the health states than the other experts.

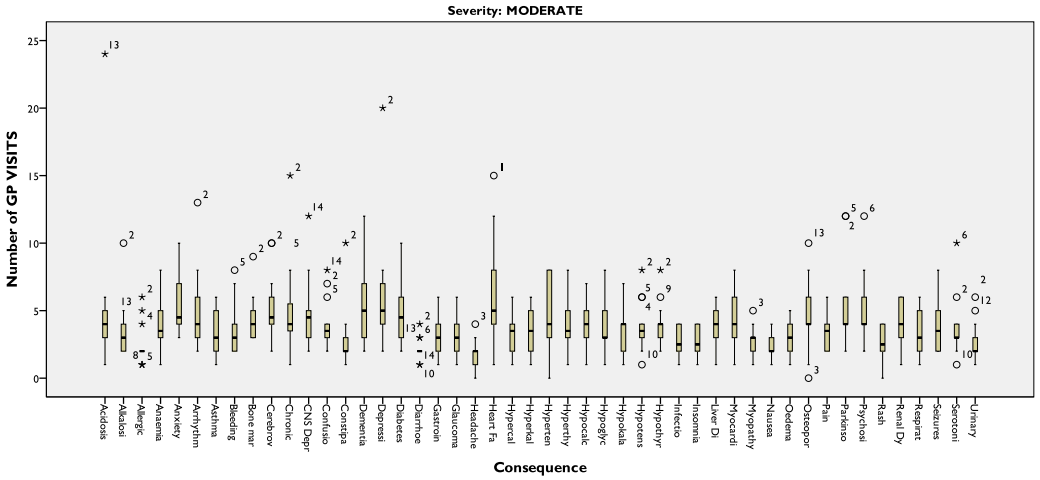

FIGURE 18 - DIFFERENCES BETWEEN EXPERTS' OPINIONS REGARDING THE NUMBER OF GP VISITS REQUIRED TO RESOLVE CONSEQUENCES AT *MODERATE* SEVERITY LEVEL. NUMBERS DENOTE RESPONSES OF INDIVIDUAL EXPERTS.

For the *Severe* health states, Expert 2's estimates of the number of GP visits were also consistently higher for many consequences (Figure 19). This was despite there being a greater spread of estimates between the remaining experts.

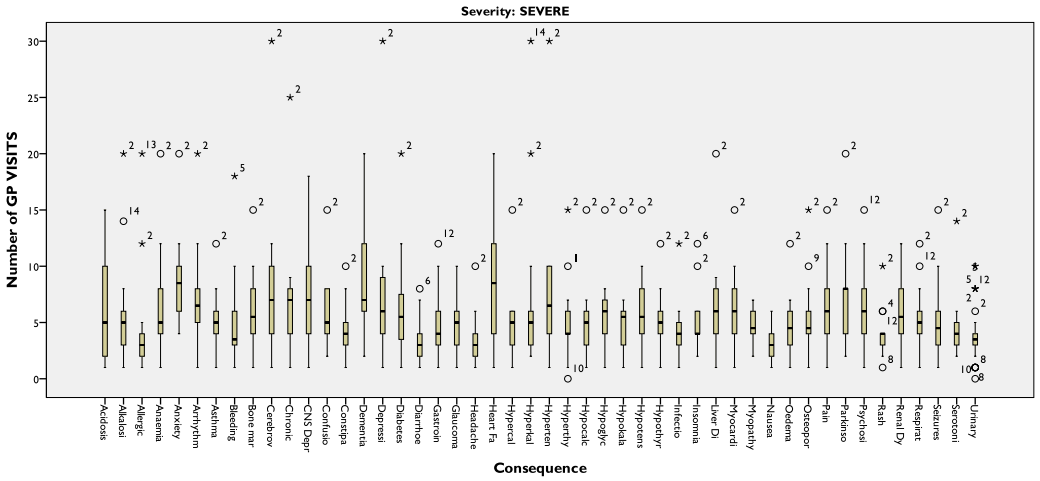

FIGURE 19 - DIFFERENCES BETWEEN EXPERTS' OPINIONS REGARDING THE NUMBER OF GP VISITS REQUIRED TO RESOLVE CONSEQUENCES AT SEVERE SEVERITY LEVEL. NUMBERS DENOTE RESPONSES OF INDIVIDUAL EXPERTS.

3.3.2.4 Specialist visits

The experts' predictions of the number of specialist visits required to resolve each health state are summarised in Table 33. In contrast to the days of ill health and number of GP visits, the variation between the experts is substantially less, especially at the lower levels of severity. At the *Mild* severity level, the median of the estimates was greater than zero for only four health states (*Cerebrovascular event*, *Glaucoma*, *Parkinsonism* and *Seizures*). In contrast, the median estimate for the *Severe* health states was at least one specialist visit for each. Consequently, for every consequence, the median number of specialist visits increased with the severity of the consequence, satisfying this requirement for validity.

TABLE 33 - EXPERT ESTIMATES OF SPECIALIST VISITS REQUIRED TO RESOLVE CONSEQUENCES AT DIFFERENT SEVERITY LEVELS

CONSEQUENCE	NUMBER OF SPECIALIST VISITS								
	SEVERITY	MILD			MODERATE			SEVERE	
	STATISTICS	MEAN ± ST DEV	MEDIAN [IQR]	RANGE	MEAN ± ST DEV	MEDIAN [IQR]	RANGE	MEAN ± ST DEV	MEDIAN [IQR]	RANGE
Acidosis		0.0 ± 0.0	0 [0]	0 to 0	1.3 ± 1.4	1 [2]	0 to 5	5.9 ± 6.7	3 [4]	1 to 25
Alkalosis		0.1 ± 0.3	0 [0]	0 to 1	1.3 ± 1.2	1 [2]	0 to 3.5	4.0 ± 3.4	3 [1]	1 to 15
Allergic reaction		0.1 ± 0.3	0 [0]	0 to 1	0.4 ± 1.0	0 [0]	0 to 3	2.3 ± 1.0	2 [1.5]	1 to 4
Anaemia		0.5 ± 0.8	0 [1]	0 to 2	1.9 ± 1.1	2 [2]	0 to 3	4.4 ± 2.6	3 [3]	1 to 12
Anxiety		0.0 ± 0.0	0 [0]	0 to 0	1.2 ± 2.3	0 [1.5]	0 to 8	4.7 ± 2.6	4 [1]	0 to 10
Arrhythmia		0.5 ± 1.2	0 [0]	0 to 4	2.5 ± 1.9	2 [2]	0 to 7	4.6 ± 2.3	4 [3]	1 to 10
Asthma		0.0 ± 0.0	0 [0]	0 to 0	0.5 ± 0.9	0 [1]	0 to 3	3.4 ± 2.5	3 [2]	0 to 10
Bleeding, non-specific		0.3 ± 0.6	0 [0]	0 to 2	1.8 ± 1.6	1.5 [1]	0 to 5	3.9 ± 3.0	3 [3]	1 to 10
Bone marrow suppression		0.5 ± 0.8	0 [1]	0 to 2	2.5 ± 1.6	3 [3]	0 to 5	5.5 ± 2.8	4.5 [2]	1 to 10
Cerebrovascular event		1.5 ± 1.3	1.5 [2]	0 to 4	2.8 ± 2.4	2.75 [4]	0 to 8	5.8 ± 4.3	5 [7.5]	1 to 16
Chronic Airways Disease		0.1 ± 0.3	0 [0]	0 to 1	1.3 ± 1.5	1.5 [2]	0 to 4	4.8 ± 3.0	4.25 [3]	1 to 12
CNS Depression		0.2 ± 0.6	0 [0]	0 to 2	1.5 ± 1.3	1 [2]	0 to 4	4.7 ± 2.9	4 [2]	0 to 10
Confusion		0.3 ± 0.6	0 [0]	0 to 2	1.1 ± 1.3	1 [2]	0 to 3	3.9 ± 3.1	3 [4]	0 to 10
Constipation		0.0 ± 0.0	0 [0]	0 to 0	0.2 ± 0.6	0 [0]	0 to 2	2.1 ± 2.4	1.5 [1]	0 to 10
Dementia		0.8 ± 1.6	0 [1]	0 to 5	2.0 ± 1.2	2 [0]	0 to 5	3.1 ± 1.9	2 [3]	0 to 6
Depression		0.2 ± 0.8	0 [0]	0 to 3	0.8 ± 0.9	0 [2]	0 to 2	5.1 ± 3.2	4 [1]	1 to 15
Diabetes		0.1 ± 0.3	0 [0]	0 to 1	0.9 ± 1.2	0 [1.5]	0 to 4	4.5 ± 2.9	3.75 [3]	1 to 12
Diarrhoea		0.0 ± 0.0	0 [0]	0 to 0	0.3 ± 0.6	0 [0]	0 to 2	2.2 ± 2.0	1.75 [2]	0 to 7
Gastrointestinal bleeding		0.3 ± 0.6	0 [0]	0 to 2	2.0 ± 1.0	2 [2]	0 to 4	3.9 ± 2.6	3 [2]	1 to 10
Gastrointestinal pain		0.0 ± 0.0	0 [0]	0 to 0	0.5 ± 0.7	0 [1]	0 to 2	2.1 ± 1.3	2 [2]	0 to 5
Glaucoma		1.2 ± 1.3	1 [2]	0 to 4	2.7 ± 1.7	3 [3]	0 to 6	4.6 ± 2.1	4.5 [3]	1 to 8
Headache		0.0 ± 0.0	0 [0]	0 to 0	0.3 ± 0.9	0 [0]	0 to 3	2.1 ± 1.7	1.5 [1]	0 to 6

Consequence	Number of specialist visits								
	Severity	Mild			Moderate			Severe	
	Statistics	Mean ± st dev	Median [IQR]	Range	Mean ± st dev	Median [IQR]	Range	Mean ± st dev	Median [IQR]	Range
Heart Failure		0.9 ± 1.4	0 [1]	0 to 5	2.1 ± 1.5	2 [2]	0 to 5	4.9 ± 3.2	4 [3]	1 to 12
Hypercalcaemia		0.3 ± 0.6	0 [0]	0 to 2	1.7 ± 1.6	1 [3]	0 to 5	4.1 ± 1.8	4 [2]	2 to 8
Hyperkalaemia		0.1 ± 0.3	0 [0]	0 to 1	0.6 ± 0.9	0 [1]	0 to 2	3.1 ± 2.1	3 [4]	0 to 7
Hypertension		0.1 ± 0.3	0 [0]	0 to 1	0.2 ± 0.6	0 [0]	0 to 2	3.8 ± 2.5	3 [3]	1 to 10
Hyperthyroidism		0.1 ± 0.3	0 [0]	0 to 1	1.6 ± 1.6	1 [3]	0 to 4	3.4 ± 1.8	3 [2]	1 to 8
Hypocalcaemia		0.1 ± 0.3	0 [0]	0 to 1	1.6 ± 1.3	2 [2]	0 to 4	3.6 ± 1.7	4 [3]	1 to 6
Hypoglycaemia		0.0 ± 0.0	0 [0]	0 to 0	0.9 ± 1.0	1 [2]	0 to 2	3.6 ± 2.1	3 [2]	1 to 8
Hypokalaemia		0.2 ± 0.6	0 [0]	0 to 2	1.1 ± 1.2	1 [2]	0 to 3	3.5 ± 1.7	3 [1]	1 to 8
Hypotension		0.0 ± 0.0	0 [0]	0 to 0	0.4 ± 0.7	0 [1]	0 to 2	3.8 ± 2.5	3 [2]	1 to 10
Hypothyroidism		0.0 ± 0.0	0 [0]	0 to 0	0.8 ± 1.2	0 [1]	0 to 4	2.6 ± 1.4	2.5 [2]	0 to 5
Infection, general		0.3 ± 1.1	0 [0]	0 to 4	0.3 ± 0.9	0 [0]	0 to 3	2.5 ± 2.8	1.5 [2]	0 to 10
Insomnia		0.0 ± 0.0	0 [0]	0 to 0	0.2 ± 0.6	0 [0]	0 to 2	1.2 ± 1.6	1 [2]	0 to 5
Liver Disease		0.2 ± 0.6	0 [0]	0 to 2	1.9 ± 1.5	2 [2]	0 to 5	4.5 ± 2.6	4 [2]	1 to 10
Myocardial Ischaemia		0.8 ± 1.2	0 [1]	0 to 4	2.0 ± 1.4	2 [2]	0 to 4	4.7 ± 2.8	4 [3]	1 to 10
Myopathy		0.1 ± 0.3	0 [0]	0 to 1	0.5 ± 1.0	0 [0]	0 to 3	1.8 ± 1.5	2 [1]	0 to 4
Nausea		0.0 ± 0.0	0 [0]	0 to 0	0.4 ± 1.0	0 [0]	0 to 3	2.2 ± 1.8	2 [1]	0 to 6
Oedema		0.0 ± 0.0	0 [0]	0 to 0	0.2 ± 0.6	0 [0]	0 to 2	3.0 ± 1.7	3 [2]	1 to 6
Osteoporosis		0.1 ± 0.3	0 [0]	0 to 1	1.2 ± 1.4	1 [2]	0 to 4	3.6 ± 1.5	3.5 [1]	1 to 6
Pain		0.0 ± 0.0	0 [0]	0 to 0	0.3 ± 0.8	0 [0]	0 to 2	4.1 ± 2.5	3.5 [3]	1 to 10
Parkinsonism		1.1 ± 1.0	1 [2]	0 to 3	2.9 ± 1.2	3 [2]	1 to 4	4.8 ± 2.5	5 [3]	1 to 10
Psychosis		0.6 ± 0.9	0 [1]	0 to 3	4.8 ± 6.0	3 [2]	0 to 24	6.8 ± 4.6	6 [3]	2 to 20
Rash		0.0 ± 0.0	0 [0]	0 to 0	0.8 ± 1.2	0 [1]	0 to 4	3.6 ± 2.3	3 [2]	1 to 8
Renal Dysfunction		0.1 ± 0.3	0 [0]	0 to 1	1.1 ± 1.1	1 [2]	0 to 3	4.1 ± 2.4	3.5 [3]	1 to 10
Respiratory depression		0.2 ± 0.4	0 [0]	0 to 1	0.8 ± 1.0	0 [1]	0 to 3	4.7 ± 5.0	3 [4]	1 to 20

Consequence	Number of specialist visits								
	Severity	Mild			Moderate			Severe		
	Statistics	Mean ± st dev	Median [IQR]	Range	Mean ± st dev	Median [IQR]	Range	Mean ± st dev	Median [IQR]	Range
Seizures		1.0 ± 1.2	0.5 [2]	0 to 4	2.1 ± 1.8	1.5 [2]	0 to 6	4.4 ± 2.8	3.5 [5]	0 to 8
Serotonin toxicity		0.1 ± 0.3	0 [0]	0 to 1	2.0 ± 3.2	1 [2]	0 to 12	2.9 ± 2.2	2 [3]	0 to 8
Urinary Incontinence		0.1 ± 0.3	0 [0]	0 to 1	1.1 ± 1.0	1 [2]	0 to 3	3.9 ± 2.4	3.5 [1]	1 to 10
Urinary retention		0.2 ± 0.6	0 [0]	0 to 2	1.3 ± 1.1	1 [2]	0 to 3	3.2 ± 1.5	3 [2]	1 to 6
Urinary Tract Infection		0.0 ± 0.0	0 [0]	0 to 0	0.0 ± 0.0	0 [0]	0 to 0	1.9 ± 1.7	1 [2]	0 to 6

The majority of the experts indicated that few of the *Mild* health states would require specialist involvement to resolve (Figure 20). Of the individual experts, Expert 12 estimated that specialist involvement would be required for several consequences where the remaining experts did not.

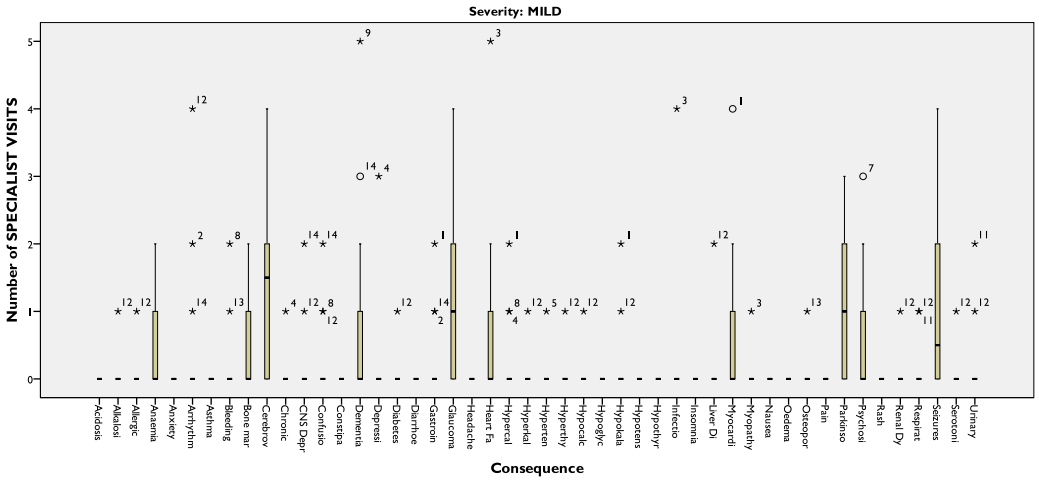

FIGURE 20 - DIFFERENCES BETWEEN EXPERTS' OPINIONS REGARDING THE NUMBER OF SPECIALIST VISITS REQUIRED TO RESOLVE CONSEQUENCES AT *MILD* SEVERITY LEVEL. NUMBERS DENOTE RESPONSES OF INDIVIDUAL EXPERTS.

In contrast, for the *Moderate* health states, Expert 12's estimates were less frequently outliers (Figure 21). There was no single expert whose estimates for this health state were consistently greater or less than the others.

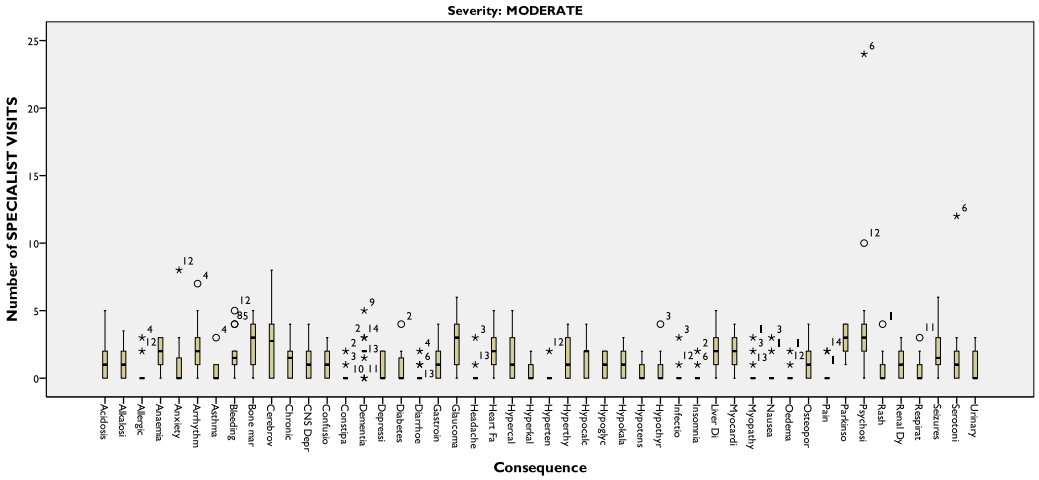

FIGURE 21 - DIFFERENCES BETWEEN EXPERTS' OPINIONS REGARDING THE NUMBER OF SPECIALIST VISITS REQUIRED TO RESOLVE CONSEQUENCES AT *MODERATE* SEVERITY LEVEL. NUMBERS DENOTE RESPONSES OF INDIVIDUAL EXPERTS.

The experts' estimates of the specialist visits required to resolve the *Severe* health states are shown in Figure 22. In general, Experts 2 and 12 estimated that more specialist visits would be required to resolve these health states than the remaining experts.

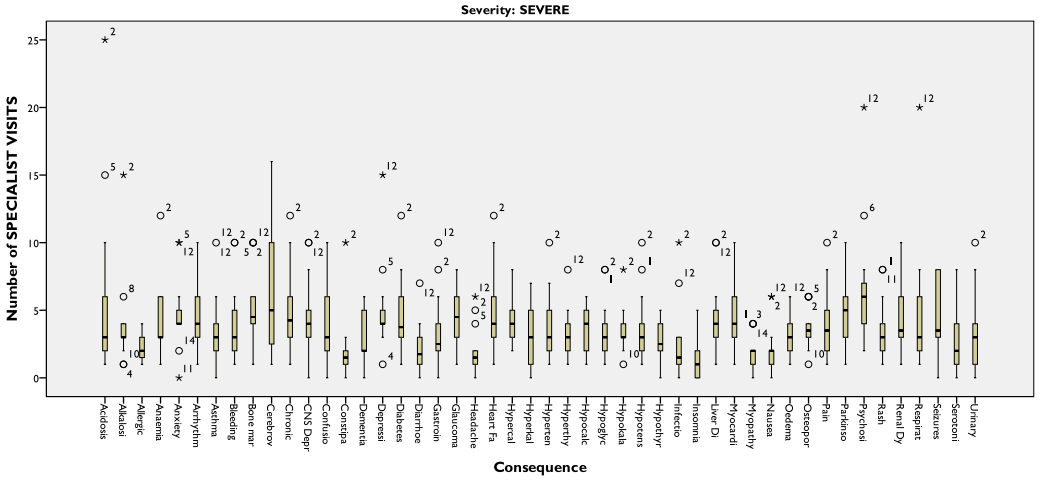

FIGURE 22 - DIFFERENCES BETWEEN EXPERTS' OPINIONS REGARDING THE NUMBER OF SPECIALIST VISITS REQUIRED TO RESOLVE CONSEQUENCES AT *SEVERE* SEVERITY LEVEL. NUMBERS DENOTE RESPONSES OF INDIVIDUAL EXPERTS.

3.3.2.5 Laboratory and pathology investigations

Responses regarding the potential laboratory investigations that would be performed were highly variable. Some provided detailed responses, whilst others were very brief. Furthermore, three of the 14 GPs did not provide details of the laboratory tests they would order as part of the management of each health state; instead they only counted how many tests they would order. Consequently, 11 opinions were obtained for pathology and laboratory tests.

The experts who responded listed 41 different pathology tests that would be used in the management of the health states. These tests, and the total number of times the tests were ordered by all of the experts are shown in Table 34.

TABLE 34 - LABORATORY AND PATHOLOGY INVESTIGATIONS ORDERED BY EXPERTS

MBS CODE	INVESTIGATION	NUMBER OF TIMES SELECTED	MBS CODE	INVESTIGATION	NUMBER OF TIMES SELECTED
55037	Abdominal ultrasound	23	66764	Faecal occult blood	14
58900	Abdominal X-ray	21	69345	Faeces MCS	21
66560	Albumin:creatinine ratio	14	65070	Full blood examination	895
59912	Angiography	25	66551	Glycosylated haemoglobin	28
66566	Arterial blood gasses	79	71079	IgE detection	14
66602	Serum B12 and folate	63	66596	Iron studies	63
69354	Blood cultures	32	66503	Lipid studies	29
66500	Blood glucose level	150	30074	Liver biopsy	4
30081	Bone marrow biopsy	18	66512	Liver function tests	232
66500	Serum calcium and phosphate	89	10942	Low vision assessment	15
55274	Carotid doppler	25	63001	Magnetic resonance imaging (head)	26
58506	Chest X-ray	194	66695	Parathyroid hormone	35
65120	Coagulation studies	39	55600	Renal ultrasound	61
32090	Colonoscopy	52	30071	Skin biopsy	7
56001	Computed tomography head	167	11506	Spirometry	64
66500	Creatine kinase	45	69318	Sputum MCS	10
12306	Dual energy X-ray absorptiometry	38	61473	Thyroid function tests	216
55113	Echocardiogram	86	66512	Serum urea, electrolytes and creatinine	995
11700	Electrocardiogram	248	69333	Urine MCS	234
11000	Electroencephalogram	25	66608	Vitamin D	11
30473	Endoscopy	58			

MCS - Microscopy, culture and sensitivity

The proportion of experts who indicated that they would order each test for each health state is shown in Appendix XVI. The experts indicated that ten of the health states would not require any laboratory or pathology investigations to resolve.

It is notable that few investigations are listed for the consequence of "Pain", with only one expert indicating that any investigations would be performed. Several experts indicated that they found the description of the consequence too broad to make accurate estimates of the investigations that would be ordered, primarily as pain may have multiple causes:

> *"Relates to cause and site"*
>
> *"Imaging depending on cause and site of pain"*

The costs of the likely investigations, as determined using the 2008 MBS, are shown in Table 35.

TABLE 35 - ESTIMATES OF COST OF INVESTIGATIONS (2008 MBS SCHEDULE)

CONSEQUENCE	SEVERITY LEVEL		
	MILD	MODERATE	SEVERE
Acidosis	$23.60	$92.06	$93.15
Alkalosis	$47.69	$66.06	$76.13
Allergic reaction	-nil-	$16.29	$42.83
Anaemia	$124.37	$414.59	$491.73
Anxiety	$5.80	$130.10	$120.80
Arrhythmia	$114.61	$249.17	$261.76
Asthma	$6.89	$32.50	$122.91
Bleeding, non-specific	$40.18	$226.98	$235.96
Bone marrow suppression	$67.45	$100.66	$180.22
Cerebrovascular event	$443.04	$479.61	$605.75
Chronic Airways Disease	$34.31	$93.51	$122.61
CNS Depression	$96.77	$250.02	$350.81
Confusion	$138.15	$226.80	$329.19
Constipation	-nil-	$90.63	$337.95
Dementia	$236.42	$350.45	$384.78
Depression	$47.03	$166.47	$235.07
Diabetes	$71.61	$102.75	$121.98
Diarrhoea	-nil-	$117.47	$127.65
Gastrointestinal bleeding	$106.50	$355.62	$365.72
Gastrointestinal pain	-nil-	$108.40	$272.66

CONSEQUENCE	SEVERITY LEVEL		
	MILD	MODERATE	SEVERE
Hyperthyroidism	$152.51	$164.00	$166.63
Hypocalcaemia	$99.71	$135.56	$162.94
Hypoglycaemia	$25.47	$84.43	$109.49
Hypokalaemia	$28.69	$72.12	$111.59
Hypotension	$46.62	$92.73	$195.26
Hypothyroidism	$137.29	$188.65	$189.54
Infection, general	-nil-	$76.87	$125.05
Insomnia	-nil-	$66.37	$73.35
Liver Disease	$30.45	$101.36	$121.10
Myocardial Ischaemia	$141.01	$415.89	$473.10
Myopathy	$17.40	$51.91	$110.36
Nausea	$1.62	$43.21	$85.68
Oedema	$12.95	$186.52	$239.72
Osteoporosis	$161.62	$159.14	$184.27
Pain	-nil-	-nil-	$3.18
Parkinsonism	$146.32	$191.65	$167.55
Psychosis	$168.17	$285.24	$312.20
Rash	-nil-	$25.60	$47.15
Renal Dysfunction	$42.99	$126.55	$176.23
Respiratory depression	$12.77	$63.20	$146.64

Glaucoma	$15.13	$23.55	$43.10	Seizures	$262.51	$416.99	$488.78
Headache	-nil-	$42.71	$224.58	Serotonin toxicity	$9.86	$64.24	$119.60
Heart Failure	$199.06	$295.64	$328.25	Urinary Incontinence	$27.63	$70.34	$85.00
Hypercalcaemia	$71.87	$152.30	$117.53	Urinary retention	$64.01	$95.91	$103.95
Hyperkalaemia	$26.50	$77.34	$110.11	Urinary Tract Infection	$11.29	$22.00	$142.77
Hypertension	$49.36	$197.68	$266.38				

For 50 of the 54 consequences (93%), the cost of investigations increased with the severity of the consequence. The four consequences that did not satisfy this criterion for validity were

- *Anxiety*, where the estimated cost of investigations for the *Severe* health state was $9.30 (7.1%) less than the *Moderate* state;
- *Hypercalcaemia* - estimated cost of investigations for the *Severe* health state was $34.77 (22.8%) less than the *Moderate* state;
- *Osteoporosis* - estimated cost of investigations for the *Moderate* health state was $2.48 (1.5%) less than the *Mild* state; and
- *Parkinsonism* - estimated cost of investigations for the *Severe* health state was $24.10 (12.6%) less than the *Moderate* state.

Given the small magnitude of the differences in the consequences of *Anxiety* and *Osteoporosis*, it may be argued that their significance is minor. Of greater concern are the discrepancies in the consequences of *Parkinsonism* and *Hypercalcaemia* as they are comparatively large.

In attempting to account for *Hypercalcaemia*, it is notable that three of the four anomalies were between the *Moderate* and *Severe* health states. This may have resulted in the experts considering that investigations would have been undertaken by a healthcare provider other than themselves; indeed, the vignettes for *Anxiety* and *Hypercalcaemia* explicitly stated that specialists would be involved in resolving the consequence. Consequently, the experts may have not listed as many investigations as they would have if they were solely responsible for managing the patient.

The vignette for *Parkinsonism* may also account for the differences seen in the estimated investigations for the *Moderate* and *Severe* health states. It may be implied from these results that the experts would attempt to investigate a patient with less advanced disease than one with severe symptoms. Given the chronic, progressive nature of Parkinson's disease, it is possible that the experts would focus on more palliative treatment of advanced disease, compared to aggressive investigation of milder presentations with the intent of confirming the diagnosis.

3.3.3 Total cost and duration

A summary of the median total estimated cost of health service utilisation and estimated duration of illness for each health state is shown in Table 36.

TABLE 36 - OVERALL ESTIMATES OF DURATION OF ILLNESS AND TOTAL COST FOR EACH HEALTH STATE IN CONSEQUENCES TABLE

CONSEQUENCE	MEDIAN OF ESTIMATES OF DURATION (DAYS) AND COST AT SEVERITY LEVELS											
	MILD		MODERATE		SEVERE		CONSEQUENCE	MILD		MODERATE		SEVERE	
Acidosis	2	$90.70	8.5	$305.31	22.5	$3 857.20	Hyperthyroidism	4.5	$202.84	8.5	$360.48	25	$6 865.28
Alkalosis	1.5	$98.02	3	$245.76	10	$3 840.18	Hypocalcaemia	2	$166.81	5	$388.51	10.5	$3 966.69
Allergic reaction	1	$33.55	3	$83.39	7	$1 555.23	Hypoglycaemia	1.5	$92.57	3.5	$264.13	7	$4 492.93
Anaemia	2.5	$191.47	12	$650.77	20	$6 129.04	Hypokalaemia	1.5	$95.79	4.5	$285.37	12	$3 111.82
Anxiety	6	$72.90	10	$281.08	22	$4 386.90	Hypotension	1.5	$113.72	6	$210.16	10	$3 752.71
Arrhythmia	4	$181.71	10	$502.12	25.5	$3 335.24	Hypothyroidism	2.5	$204.39	8.5	$322.85	12.5	$4 346.75
Asthma	4	$57.22	7	$133.15	14.5	$3 643.78	Infection, general	2	$33.55	7	$160.75	17	$3 867.10
Bleeding, non-specific	2	$73.73	5	$426.53	14	$3 922.02	Insomnia	2	$33.55	6	$150.25	14	$286.60
Bone marrow suppression	3	$151.33	7	$393.31	27	$2 713.59	Liver Disease	0.5	$80.78	5	$354.31	21.5	$4 578.59
Cerebrovascular event	3	$659.37	8.5	$3 951.74	60	$8 980.04	Myocardial Ischaemia	3	$208.11	8.5	$2 132.84	30	$6 287.16
Chronic Airways Disease	4	$134.96	12	$326.61	30	$5 535.18	Myopathy	2	$50.95	4.5	$152.56	10	$396.86
CNS Depression	3	$163.87	14	$480.05	27.5	$10 403.58	Nausea	2	$35.17	4	$110.31	7	$3 742.93
Confusion	4	$205.25	10	$423.28	25	$6 318.37	Oedema	1	$46.50	5.5	$287.17	17	$5 973.92
Constipation	2.5	$33.55	6	$157.73	12	$4 109.22	Osteoporosis	1.5	$228.72	14	$372.39	30	$4 020.89
Dementia	10.5	$337.07	30	$636.95	365	$5 571.09	Pain	2.5	$33.55	10	$117.43	22	$7 576.38
Depression	4	$114.13	14	$334.22	55	$8 566.56	Parkinsonism	7	$309.25	30	$484.30	200	$5 506.51
Diabetes	3	$172.26	7	$253.73	20	$4 731.51	Psychosis	4.5	$235.27	17	$577.89	60	$11 474.38
Diarrhoea	2	$33.55	7	$1 685.57	10	$3 167.13	Rash	2	$16.78	6	$109.48	17.5	$2 560.49

Consequence	Median of estimates of duration (days) and cost at severity levels											
	Mild		Moderate		Severe		Consequence	Mild		Moderate		Severe	
Gastrointestinal bleeding	1	$173.60	7	$591.80	14	$5 255.37	Renal Dysfunction	1	$110.09	6	$339.80	25.5	$6 950.88
Gastrointestinal pain	2.5	$33.55	8.5	$209.05	14.5	$3 501.76	Respiratory depression	2	$63.10	8.5	$163.85	25	$4 041.36
Glaucoma	2	$161.28	5	$282.65	15	$1 994.85	Seizures	2	$369.14	5	$633.32	20	$3 615.34
Headache	1	$0.00	4.5	$109.81	10	$5 942.24	Serotonin toxicity	2	$43.41	7	$243.94	12	$372.55
Heart Failure	5	$282.94	20	$582.14	45	$4 266.20	Urinary Incontinence	2	$61.18	10	$250.04	30	$2 951.90
Hypercalcaemia	2	$122.20	5	$348.78	14.5	$4 965.05	Urinary retention	2	$97.56	5	$275.61	10	$4 555.72
Hyperkalaemia	1	$93.60	4.5	$194.77	12	$3 076.79	Urinary Tract Infection	1	$44.84	4	$55.55	10	$3 967.02
Hypertension	0	$116.46	2.5	$331.88	14	$3 127.39							

3.3.4 Distributions fitted

The distributions and the parameters describing them for each health state are shown in the complete consequences table (Appendix XVII). A summary of the results of the distribution analysis is presented in Table 37. For the three parameters for which the distribution process was performed, best-fit distributions were the most frequently identified.

TABLE 37 - RESULTS OF DISTRIBUTION FITTING FOR EXPERT ESTIMATES OF PARAMETERS LINKED TO CONSEQUENCES

DISTRIBUTION	PARAMETER		
	DAYS OF ILL HEALTH	NUMBER OF GP VISITS	NUMBER OF SPECIALIST VISITS
Number of best fit distributions			
• Beta general	75		
• Binomial		39	22
• Negative binomial		43	31
• Poisson		57	28
• Geometric		6	37
Number of degenerate distributions			
• Calculated beta	55	8	17
• Fixed average	23	0	0
No distribution fitted (100% agreement between experts)			
	0	0	18
TOTAL	**153**	**153**	**153**

3.3.5 Validity

3.3.5.1 Correlation between cost and duration of illness

To provide an indication of the validity of the results, the correlation between the duration of illness and the costs associated with resolving each health state was investigated. It was assumed that significant positive correlation between these parameters would suggest that the estimates were generally valid.

The relationship between these parameters was investigated using Pearson product-moment correlation coefficient and Kendall's non-parametric test. Both tests indicated that there was a strong correlation between the duration of illness and the costs

associated with resolving each health state (r=0.41, n=153, *P*<0.001, tau-b value=0.67, *P*<0.001).

This relationship is illustrated in Figure 23.

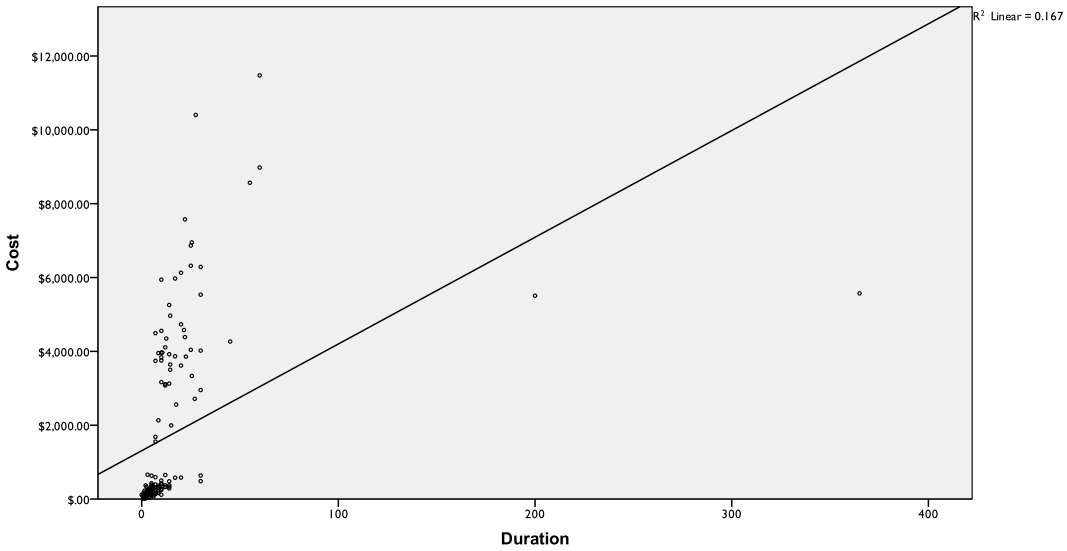

FIGURE 23 - SCATTERPLOT ILLUSTRATING THE RELATIONSHIP BETWEEN ESTIMATES OF DURATION OF ILLNESS (DAYS) AND TOTAL HEALTH RESOURCE UTILISATION COSTS

3.3.5.2 Comparison with previous consequences table

The estimates of the duration of illness and healthcare service utilisation costs associated with each health state derived in the study were compared to those obtained for Tenni's consequences table. As the two tables were derived using different methodologies it was anticipated that there would be some differences in the outcomes. This was found to be the case, as discussed below.

3.3.5.2.1 Days of ill health

The estimates of the duration of illness developed by Tenni were multiples of one week; hence the shortest duration of illness was 7 days, and the longest was one year. In contrast, as discussed in Section 3.3.2.2, the experts in this new study considered that several of the health states were unlikely to result in any symptomatic ill health

whatsoever, especially at the *Mild* severity level. Consequently, the estimates for the duration of ill health were highly disparate at the *Mild* severity level, with Tenni's estimates all substantially greater than those derived in the new study (Figure 24).

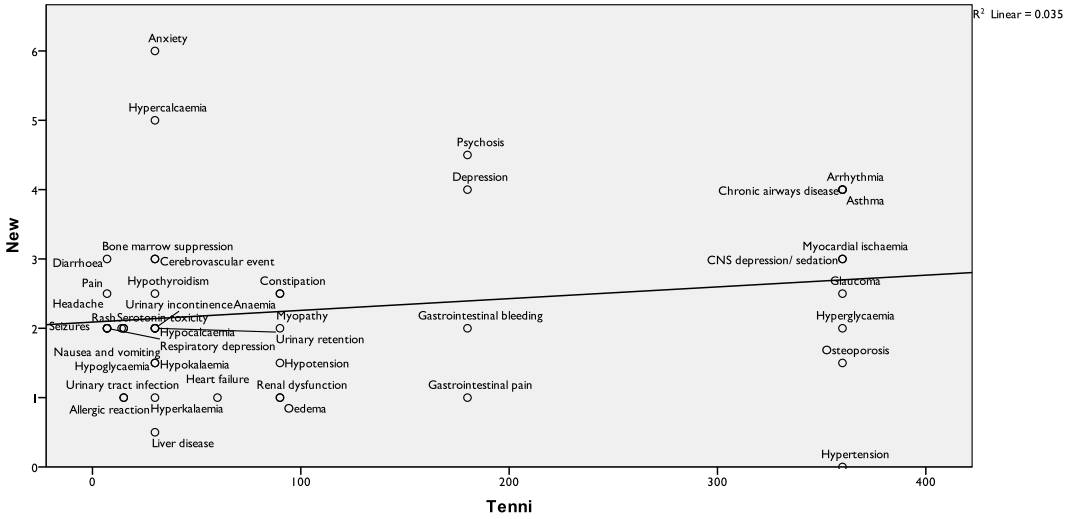

FIGURE 24 - ORIGINAL AND NEW ESTIMATES OF DURATION OF ILLNESS FOR MILD SEVERITY HEALTH STATES (DAYS)

The differences in the estimates for the *Moderate* health states were similar to that observed in the *Mild* states, with each of the new estimates being shorter than those derived in the earlier study (Figure 25).

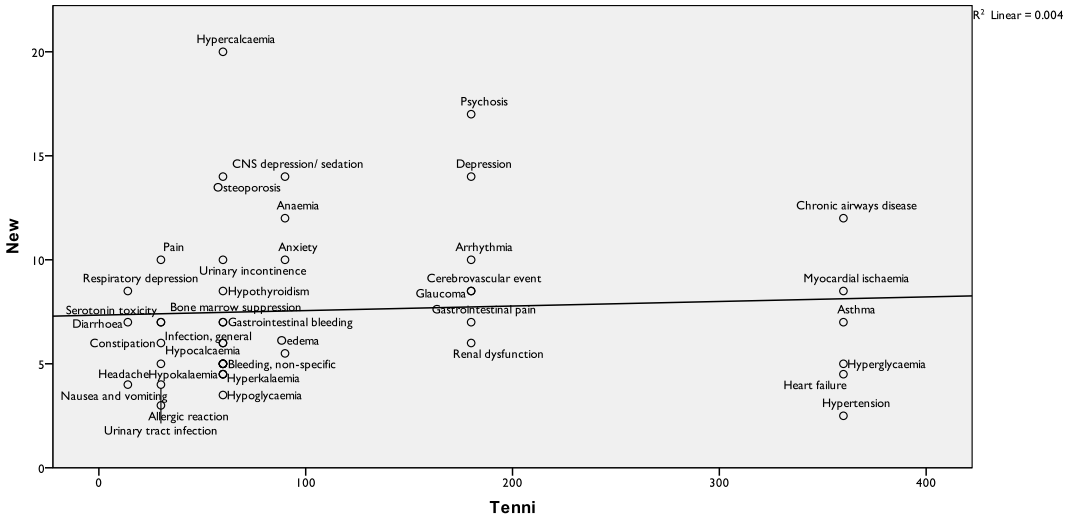

FIGURE 25 - ORIGINAL AND NEW ESTIMATES OF DURATION OF ILLNESS FOR MODERATE SEVERITY HEALTH STATES (DAYS)

The differences between the two data sets were least apparent between the *Severe* health states (Figure 26). However, each of the newer estimates remained of a shorter duration than those derived by Tenni.

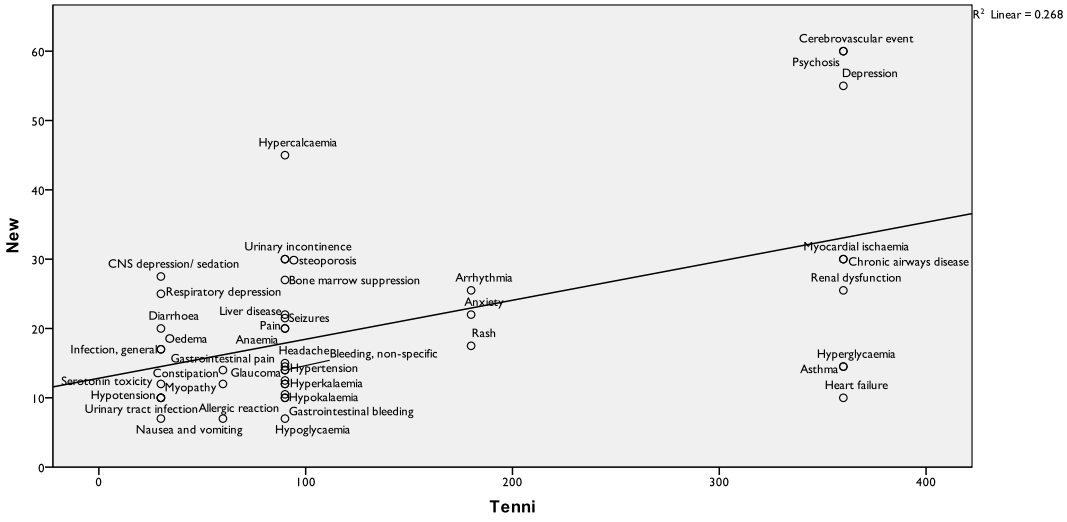

FIGURE 26 - ORIGINAL AND NEW ESTIMATES OF DURATION OF ILLNESS FOR SEVERE SEVERITY HEALTH STATES (DAYS)

3.3.5.2.2 Total healthcare utilisation costs

In contrast to the estimates for duration of illness, the estimates for the total healthcare utilisation costs were generally greater in the new study compared to the original study. At the *Mild* severity level, all but six consequences were estimated to result in greater healthcare utilisation costs in the new study compared to the earlier study (Figure 27). Of these six consequences, the estimate for *Gastrointestinal bleeding* showed the greatest discrepancy. This was primarily due to the earlier study including endoscopy as an investigation, whereas only two of the 11 experts in the new study indicated that this procedure would be performed to manage this health state.

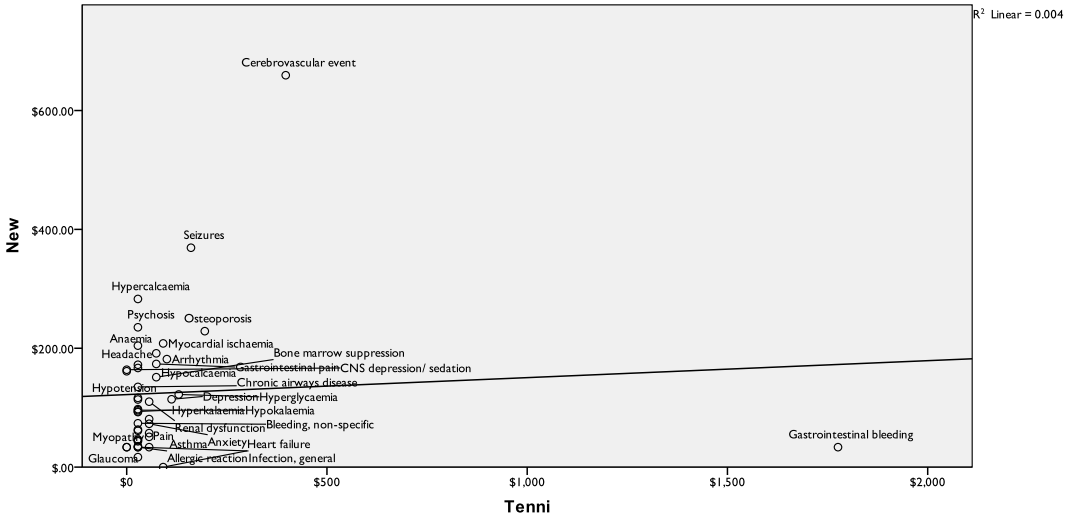

FIGURE 27 - ORIGINAL AND NEW ESTIMATES OF COST OF HEALTHCARE UTILISATION FOR MILD SEVERITY HEALTH STATES

At the *Moderate* severity level, the estimated total healthcare utilisation costs were greater in the new study for all but nine of the health states (Figure 28).

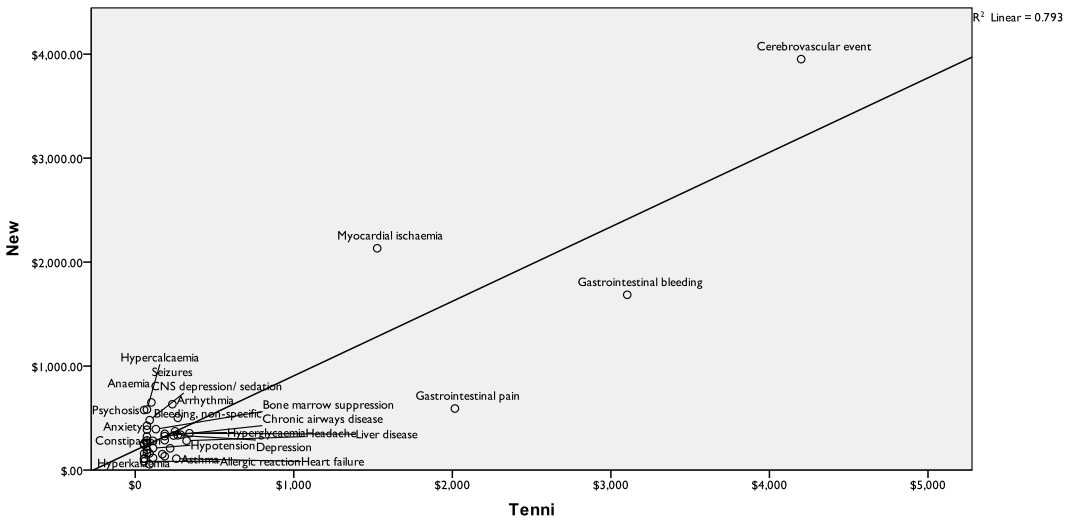

FIGURE 28 - ORIGINAL AND NEW ESTIMATES OF COST OF HEALTHCARE UTILISATION FOR MODERATE SEVERITY HEALTH STATES

Seven of the new estimates of the total healthcare utilisation cost for the *Severe* health states were less than those in the original study (Figure 29).

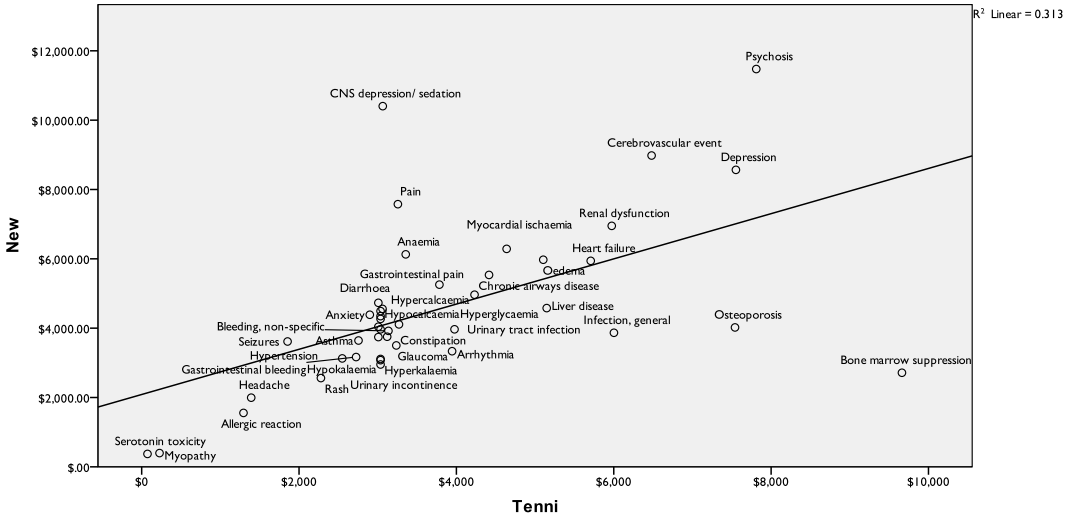

FIGURE 29 - ORIGINAL AND NEW ESTIMATES OF COST OF HEALTHCARE UTILISATION FOR SEVERE SEVERITY HEALTH STATES

A summary of the differences between the estimates of the total cost of health resource utilisation and duration of illness produced by the two studies is shown in Table 38.

TABLE 38 - SUMMARY OF DIFFERENCES IN ESTIMATES OF TOTAL HEALTH RESOURCE UTILISATION COSTS AND DURATION OF ILLNESS

PARAMETER	ORIGINAL STUDY		NEW ESTIMATES*	
	MEDIAN (IQR)	RANGE	MEDIAN (IQR)	RANGE
Total cost of health resource utilisation ($)				
• Mild	28.02 (45.82)	0 - 1776.06	98.01 (135.21)	0 - 659.36
• Moderate	112.06 (174.93)	56.03 - 4200.09	305.31 (231.76)	55.55 - 3951.74
• Severe	3092.07 (1574.50)	73.83 - 9662.71	4041.36 (2235.85)	286.6 - 11474.38
Duration of ill health (days)				
• Mild	30 (161.25)	7 - 360	2 (1.5)	0 - 10.5
• Moderate	60 (120)	14 - 360	7 (5)	2.5 - 30
• Severe	90 (120)	30 - 360	17 (13.5)	7 - 365

*median of estimates made by 14 experts (see text)

3.4 Discussion

The primary aims of this study were to update the healthcare utilisation costs in Tenni's consequences table, and to estimate the uncertainty of the imprecise costs. Whilst these aims were generally achieved, uncertainty regarding the estimates was noted for many of the valued health states, resulting from substantial variability between the experts' opinions. Additionally, the study failed to capture the uncertainty regarding the cost of the laboratory and pathology investigations that may have been involved in the management of each health state.

It was unsurprising that there were substantial differences between the experts with regard to their estimates of many of the parameters in this study, given the inherent imprecisions of expert opinion. To achieve perfect agreement between the experts would have required each expert to interpret the health states and their vignettes identically, and then predict very similar, if not identical, clinical courses for the health state to be resolved. However, it is recognised that differences between clinicians will

influence their choice of therapy for the same patient, even in the context of compelling indications for a particular therapeutic decision.[229]

For example, for the consequence of *Allergic reaction*, one expert commented,

> *"Allergy is common and rarely needs specialist involvement except at the extreme end" (Expert 13).*

In contrast, for the same consequence, another expert stated that they,

> *"Would refer to allergy clinic at Moderate [severity level]" (Expert 12)*

Consequently, Expert 12 estimated that consequence would result in specialist visits at both *Moderate* and *Severe* levels, whereas Expert 13 only indicated specialist visits would result from the *Severe* level. It is therefore likely that these differences in practice were responsible for much of the variability between then experts. Moreover, this illustrates the value of representing the experts' opinions as distributions instead of point estimates to encapsulate the variability between the experts.

Another cause of differences between the experts' estimates may have resulted from the lack of any clinical context for each of the health states. Each expert was asked to make their predictions based on the assumption that the described health states resulted from medication use (such as adverse effects). However, in the absence of further information about an individual patient's medical history or clinical status, this would have required the experts to make assumptions about these parameters to make their estimates. Several experts made comments that this factor complicated the assessment process, for example:

> *"This is a very difficult exercise when there is so little information."(Expert 1)*

> *"Difficult to answer as really depends on the cause" (Expert 13)*

A solution to this issue may have been to generate multiple scenarios where different patients experienced the same health state and for the experts to estimate the relevant healthcare utilisation parameters for each. However, whilst this may have improved the accuracy of the estimates, the scope of the study would have had to have

been greatly increased, given the large number of different scenarios that would likely have needed to be evaluated by the experts.

In addition to the variability between the opinions of the experts in this study, substantial differences were observed between the results of this study and those observed by Tenni in the original study. In general, the estimates of the duration of ill health in this study were shorter than those in the first study, whereas those for the cost of health service utilisation were higher. With regards to the differences in the estimates of the health resource utilisation costs between the two studies, it is likely that price increases over time may have accounted for some of the differences observed. Tenni used hospitalisation data from 2002-3 and the 2005 MBS schedule to cost the original table; this new study used hospitalisation data from 2006-7 and the 2008 MBS schedule.

A second potential reason for these differences is that the studies used different methods to develop the estimates. In this new study, the experts participated in isolation and mathematical aggregation was used to combine their estimates, whereas consensus was achieved using informal behavioural aggregation in the original study. There is little, if no literature that has investigated which technique produces more robust results. Furthermore, in consideration of the inability to validate either study's results with real-world data means that any suggestion that the one study's estimates are more reliable than the other is purely conjecture. However, it may be argued that the increased number of participants in this new study and the representation of the parameter estimates as distributions rather than point estimates are likely to have resulted in more appropriate estimates than the original study.

The magnitude of the differences between the estimated durations of illness between the two studies is concerning, and raises questions about the value of comparing this aspect of the two datasets. Moreover, it is difficult to interpret these findings as the documentation of the development of Tenni's consequences table is minimal.[xv] It is

[xv] The only documentation of how the estimates for the parameters involving non-admission treatment were developed by Tenni is as follows: "*The initial estimates for these parameters were made and then reviewed and modified by a consensus group process that included a physician, a general practitioner and two experienced clinical pharmacists*."[204]

possible that the experts provided their estimates in different contexts. For example, in this new study, the experts were asked to estimate the duration of ill health for each health state. Had they been asked to estimate the health resource utilisation resulting from a pre-defined duration of illness, it is possible that their responses may have been much different. However, as the estimated costs associated with the health states were generally greater in this study than that by Tenni, it seems unlikely that this reason could account for the disparity. Perhaps the most appropriate conclusion from this aspect of the study is that it is imperative for any subsequent research that uses a similar methodology to explicitly state *what* each expert was asked to estimate, in addition to *how* the estimates were obtained.

In the absence of further details of the methodology used to develop Tenni's consequences table, it is not possible to draw definitive conclusions regarding which study developed more reliable estimates of the parameters of interest. However, it may be argued that the methodology used in the new study was substantially more robust and transparent than that used in Tenni's research, and addressed several major limitations of the original consequences table. In addition to a greater number and broader spectrum of clinicians being involved, the new study developed both estimates of the parameters of interest and the uncertainty regarding each estimate. Based on these considerations, it may be argued that the research presented in this chapter is an important development of the consequences table pioneered by Tenni, and more appropriate to be used in economic evaluations.

The most significant limitation to the results of this study was the inability to validate the estimates of many of the parameters measured with real-world data. The results of the correlation analysis and testing of coherence suggests that they are generally plausible and coherent estimates. However, the results cannot be considered to be reliable, validated and accurate estimates of each parameter. The differences between the experts' opinions demonstrate the significant uncertainty regarding the estimates of each parameter. There is a clear need to use uncertainty analysis when using these results in an economic evaluation. A focus of further work in this area should involve investigating the validity of these findings, such as by comparing them to real-world data (such as the BEACH database)[224] or systematic literature reviews. Such research may also clarify, to some extent, which type of consensus methodology is more suited to this type of application.

To gauge the uncertainty of the estimates, PSA was used to characterise the distribution *between* each expert's opinions for each parameter they assessed. However, this resulted in a second limitation as no uncertainty *within* each expert's opinion for each parameter was measured, meaning that overall uncertainty is almost certainly under-represented in the results. A potential solution to this issue would have been for each expert to estimate a probabilistic distribution for each parameter, rather than a point estimate of the most-common scenario. Recent literature has demonstrated the plausibility of such an approach.[230] However, this would have been significantly more complex and time-consuming than the method used in this study, and there is no literature to support the theory that distribution estimation is more appropriate than aggregating point estimates. It is plausible that this limitation will have only slight practical implications, since in a heavily re-sampled estimate the incidences where any given estimate is slightly lower are likely to be largely offset by the incidences where the estimate is higher, and vice versa.

A further limitation results from the use of DRG data to estimate hospitalisation costs and length of stay. By definition, this data represents the average cost and length of stay for a number of clinically similar, not identical, admissions. Depending upon factors such as patient characteristics and geographical location, the value of these parameters may differ considerably. Despite this limitation, this data is frequently used in economic analyses and should not substantially impact upon the accuracy of the estimates of hospitalisation costs and duration of admission.

Finally, a methodological limitation that remains to be overcome is that drug costs relating to the health states are not accounted for in the methodology. These costs may account for a significant portion of the total cost of the management of the health states, and their exclusion may result in an underestimate of the total cost or saving of an intervention. These costs were purposely excluded by Tenni as it was considered that incorporating them would add an unacceptable level of uncertainty into the model.[204] Whilst this may be the case, the results of this study illustrate that there is considerable uncertainty in most of the parameters investigated. It is possible that the uncertainty introduced by considering drug costs may not be greater than that which is already present. Future work involving this methodology should therefore investigate the potential for adding drug costs to each consequence.

Despite these limitations, the study developed estimates of the costs and their uncertainty resulting from health resources utilised by each of the health states described in Tenni's consequences table. Having undertaken this work, the results from economic analyses generated using Tenni's methodology should be considered more robust than those obtained using the original consequences table estimates.

Chapter 4 - Measuring quality of life

4.1 Introduction

The methodology developed by Tenni involved the assignment of a level of "health-status impact" to each health state.[204] This was an arbitrary scale of the effect of each health state on QOL, with 1 being *Mild* impact on health, 2 being *Moderate* impact and 3 being *Severe* impact on health. Essentially, this measure assumed that at the same severity level, any given consequence has the same effect on QOL as every other consequence experienced at that severity level.

This assumption is inconsistent both intuitively and in the health economic literature. To illustrate, consider the QOL effects of the *Mild* level of the consequences *bleeding* and *cerebrovascular ischaemia*. According to Tenni's methodology, the QOL of a patient with minor bruising is equivalent to the QOL of a patient experiencing a temporary ischaemic attack. Clinicians familiar with both of these health states would most likely agree that this is an unreasonable assumption. Furthermore, this methodology does not readily permit direct comparisons between different interventions as there is no standardised humanistic outcome measure.

Most commonly, in health economic literature, the influence of a particular disease or condition on QOL is expressed in terms of *utility* (*Q*, also referred to as *quality weights*, *preference weights* or *preference values*).[231] These utility weights reflect the desirability of residing or existing in a particular health state. Typically, each health state is rated on a scale from 1.0 (the best health attainable) to 0 (dead).[xvi] Examples of utilities that have been reported for various conditions are shown in Table 39.

[xvi] Some systems, such as the EQ-5D, permit health states to be rated at less than 0, or "worse than death"

TABLE 39 - EXAMPLES OF UTILITIES REPORTED FOR VARIOUS MEDICAL CONDITIONS
232

CONDITION	UTILITY	CONDITION	UTILITY
Osteoarthritis of the hip		Stroke resulting in cognitive deficit	
• Mild	0.69	• Mild	0.54
• Moderate	0.38	• Moderate	0.37
• Severe	0.19	• Severe	0.08
Angina		Chronic hepatitis	0.94
• Mild	0.88		
• Moderate	0.832	Chronic renal disease	0.63
• Severe	0.533		

The QOL outcome unit most frequently reported in cost-utility analyses is the QALY.[182] QALYs are calculated by summing the time spent in a health state weighted by the utility value associated with the health state.[233] QALYs therefore incorporate both length of survival and utility into a single metric. A related measure is the disability adjusted life year (DALY). In a similar fashion to the utility weights of QALYs, DALYs are also calculated using measures of QOL anchored between 0 and 1, termed disability weights (*D*). A fundamental difference between *Q*s and *D*s, however, is that a *D* of 0 indicates full health and a *D* of 1.0 is equivalent to death. This inversion is because the QALY measures equivalent healthy years lived, whereas the DALY measures years of lost health. The *D* for a given condition *i* may therefore be converted to a *Q* using Equation 2, and vice versa.

$$Q_i = 1 - D_i$$

EQUATION 2 - CONVERSION OF D WEIGHTS TO Q WEIGHTS

It therefore seems possible that a way to overcome this limitation in Tenni's methodology is to assign utilities to every health state. This would have the additional benefit of facilitating a cost-utility analysis, enabling the provision of QALYs as an additional outcome measure. This is desirable as many agencies (such as Australia's

Pharmaceutical Benefits Advisory Committee, PBAC, and the UK's National Institute for Health and Clinical Excellence, NICE), now prefer or require economic evidence of the health benefits of an intervention to be quantified in QALYs.[234-236]

The aim of this study was to assign utilities to the health states. The following section details the methodological considerations that were made to ensure appropriateness and robustness of the utilities assigned.

4.2 Methods

4.2.1 Utility sets

The initial consideration in undertaking this study was whether to measure utilities (using either direct or indirect measures), or to use literature values. The gold standard for obtaining utilities from most economists' viewpoints is direct measurement using an approach such as standard gamble (SG), time trade-off (TTO) or person trade-off (PTO).[237] SG involves respondents making a choice between two alternatives called alternatives 1 and 2.[238] In alternative 1, there is a probability that two possible outcomes may occur: either the patient returns to full health and lives for a number of additional years, or they die immediately. Alternative 2 involves the patient living with the health state being valued for a different number of additional years, with no uncertainty. The probability of full health versus death in alternative 1 is then varied until the respondent is indifferent between alternatives 1 and 2. Typically, SG measurements are obtained using one-on-one interviews, detailed interview scripts and visual aids.[238]

Similarly to SG, TTO involves respondents being asked to choose between two alternatives.[237] However, in contrast to SG, both alternatives have certain prospects, namely years in full health, and years in the health state being valued (which is longer than the years in full health). The respondent then considers trading reductions in length of life for health improvement, until they are indifferent to the two alternatives. PTO is similar to TTO, except that respondents essentially make choices in the context of other people, rather than themselves.[237]

In reality, these techniques are time consuming and complex as they generally require a trained interviewer to explain the concept to the respondent without leading them or distressing them if the respondent is a patient with the condition. As there were 153 health states to be valued in this study (51 consequences, each at three levels of severity), this would have been a major undertaking. Furthermore, such a project was potentially unnecessary, as several large studies had already developed utilities using one of these techniques.

Most DALY calculations are based on universal sets of standard weights derived using expert valuations.[239] For example, the World Health Organisation 1990 Global Burden of Disease (GBD) study developed a set of disability weights using a PTO technique to provide estimates of lost health due to 107 disease-related causes in terms of DALYs.[240] Researchers from the Netherlands modified the GBD study PTO methodology in the "Dutch weights" study.[241] The Dutch weights study derived disability weights for 52 diseases of public health importance to western European nations. Not only did this study provide disability weights for these diseases, it also weighted the disability of different *stages* or *severity levels* of many of these diseases. The study ultimately provided disability weights for 175 different disease stages, sequelae or severity levels for the 52 diseases. These utilities were utilised in the Australian Burden of Disease and Injury (ABDI) studies to estimate the health lost due to disease and injury in Australia.[242, 243]

As these utility sets had been developed using methodologically robust techniques and they had been used in an Australian context, it was considered that they were suitable utilities for the study to be undertaken in this research. Hence, the first objective for the study was to investigate the consequences for which Dutch weights or GBD utilities could be assigned (i.e. when the descriptions approximated the vignettes developed for each consequence). As the Dutch weights were developed specifically for Western nations rather than a global context (as per the GBD weights), they were used as a primary reference. For the health states that were not described by the Dutch weights, the GBD utilities were used where appropriate.

The validity of this approach was investigated by Mathers *et al.* who compared the Dutch weights to GBD weights for 54 conditions.[242] They found a correlation

coefficient between these weights of 0.91 (Figure 30), and concluded that using both Dutch and GBD weights in the same study was a reasonable approach.

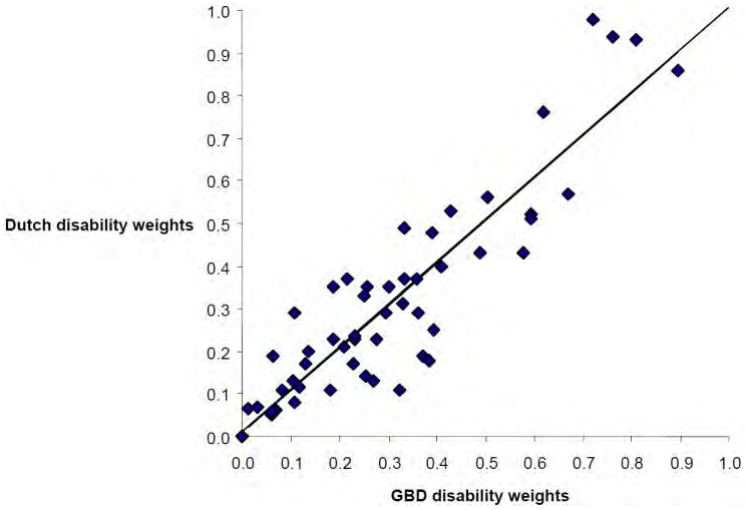

FIGURE 30 - COMPARISON OF GBD AND DUTCH WEIGHTS FOR 54 COMPARABLE DISEASE AND INJURY CATEGORIES. REPRODUCED FROM MATHERS *ET AL.* [242]

A second approach used by Mathers *et al.* to calculate utilities for conditions using the GBD and Dutch weights was to take averages when multiple weights were available for a particular condition.[242] For example, to obtain a utility for *"Schizophrenia"*, they used a composite of the GBD weights for *"Psychosis"* and *"Treated schizophrenia"*. In consideration of this, averages of weights were calculated for health states whose descriptions were aligned with two or more reference weights.

However, it was anticipated that these approaches would not completely facilitate the assignment of utilities to every health state. This was because the GBD, ABDI and Dutch weights primarily value QOL of chronic diseases, whereas the consequences table involved many acute conditions with minor impact on QOL. If literature values for these utilities were to be used, an alternative source of utilities was required.

4.2.2 Alternative sources of utilities

4.2.2.1 Potential literature sources

There are databases that provide utilities derived in QOL assessments in different studies,[244] and summaries of studies that reported utilities for numerous medical conditions have been published.[232] However, choosing utilities that approximated the consequences from these references was inappropriate, primarily because a variety of techniques have been used to determine utilities in these studies. Utilities derived from one technique often do not directly equate to utilities obtained using an alternate technique.[182, 237] For example, in their review of 1000 QOL estimates, Tengs *et al.* identified five utilities for the health state of "myocardial infarction" (Table 40). Depending upon the method used, the variability between utilities (i.e. the QOL loss incurred by the condition) was greater than three-fold.

TABLE 40 – REFERENCE UTILITIES FOR "MYOCARDIAL INFARCTION"[232]

ASSESSMENT METHOD	LOWER BOUND*	UPPER BOUND*	UTILITY
Rating scale	Death	Perfect health	0.68
Rating scale	Death	Perfect health	0.7
Rating scale / Time trade-off	Death	Excellent health	0.72
Time trade-off	Death	Excellent health	0.87
Judgement	Death	Excellent health	0.9

* indicates the best and worst possible health state following myocardial infarction

Given the variability between literature values derived using different methods, it was decided to investigate the potential for developing utilities specifically for the study using another technique. As stated previously, direct utility measurement (using SG, TTO etc) is complex and time-consuming. An alternative that is used extensively in health economic literature is to use a pre-scored multi-attribute health status classification system. These systems use a variety of means (usually questions relating to QOL) to map responses to the system to value sets derived by one of the direct utility measurement techniques. Multi-attribute health status classification system instruments may be either generic or disease-specific. Generic heath status instruments allow the comparison of QOL between essentially any different disease or

condition, whereas disease-specific instruments are limited to the diseases which they were developed to assess.

Both types of instruments assess several different aspects of the patient's health status (termed "domains"). These domains typically include physical functioning, psychological functioning, social role and functioning, and general health perceptions.[182] The instrument may report the patient's health status as different scores for each domain or as a single summary index.

4.2.2.2 The EuroQOL 5D

One of the most widely used generic health status instruments is the EuroQOL (EQ-5D).[245] It was developed to provide a simple, generic measure of health for clinical and economic assessments, and a modified version of the EQ-5D was used in determining the Dutch weights.[241] The EQ-5D consists of two pages: a visual analogue scale and a descriptive system. The descriptive system, shown in Figure 31, assesses QOL in five domains - mobility, self-care, usual activities, pain/discomfort and anxiety/depression. Each domain is described by three levels of health impact– no problems (level 1), some problems (level 2) and severe problems (level 3). Respondents are asked to indicate which level best describes their health status for each domain. The five individual responses may then be combined into a five digit number that describes the respondent's health state. For example, a patient who responds that they have no problems with mobility, self-care or usual activities, but severe pain and moderate anxiety, would be summarised as *11132*. As each of the five domains has three possible responses, there are 243 possible health states that can be defined by the instrument.

BY PLACING A TICK IN ONE BOX IN EACH GROUP BELOW, PLEASE INDICATE WHICH STATEMENTS BEST DESCRIBE YOUR OWN HEALTH STATE TODAY

MOBILITY

I have no problems in walking around	☐
I have some problems in walking around	☐
I am confined to bed	☐

PERSONAL CARE

I have no problems with personal care	☐
I have some problems washing or dressing myself	☐
I am unable to wash or dress myself	☐

USUAL ACTIVITIES (E.G. WORK, STUDY, HOUSEWORK, FAMILY OR LEISURE ACTIVITIES)

I have no problems with performing my usual activities	☐
I have some problems with performing my usual activities	☐
I am unable to perform my usual activities	☐

PAIN/DISCOMFORT

I have no pain or discomfort	☐
I have moderate pain or discomfort	☐
I have extreme pain or discomfort	☐

ANXIETY/DEPRESSION

I am not anxious or depressed	☐
I am moderately anxious or depressed	☐
I am extremely anxious or depressed	☐

FIGURE 31 - EQ-5D DESCRIPTIVE SYSTEM [245]

Responses to the EQ-5D descriptive system may be mapped to utilities using a value set based on the responses of a general population. These tariffs were developed in previous separate studies in which various possible health states have been calibrated by means of a trade-off method from a sample of the general population.[236] Whilst there are value sets for several countries, currently a value set has not been created for the Australian population. Many Australian studies have therefore used the UK TTO value set, as this population's demographics are closest to that of Australia's.[245] EQ-5D descriptive system responses may be mapped to UK TTO utilities using Equation 3. The utility derived from this equation does not quantify the respondent's value of their own health, but rather the value that the general population would place on the respondent's health.

$$Q = 1 - 0.081 - 0.069M_2 - 0.314M_3 - 0.104S_2 - 0.214S_3 - 0.036U_2 - 0.094U_3 - 0.123PD_2 - 0.386P_3 - 0.071A_2 - 0.236A_3 - 0.269N_3$$

M_X = mobility S_X = self care U_X = usual activities P_X = pain/discomfort
A_X = anxiety/depression N_3=1 if one or more "severe" responses, 0 if nil

EQUATION 3 - CONVERSION OF EQ-5D DESCRIPTIVE SYSTEM RESPONSES TO UK TTO UTILITIES

Given its wide usage in the Australian context, it was decided to use the EQ-5D mapped to UK TTO values to measure utilities for the health states for which Dutch, ABDI or GBD weights were unavailable.

4.2.2.3 Anchor points

A complication with using this methodology is that, unlike the GBD, ABDI and Dutch weights, the UK TTO values are not anchored between 0 and 1; in fact, 81 out of the 243 health states described by this value set have utilities less than 0 (Figure 32). This reflects that being in one of these 81 health states is "worse than death". Conversely, the GBD, ABDI and Dutch weights are anchored between 0 and 1, and so are not directly comparable to weights derived using the EQ-5D.

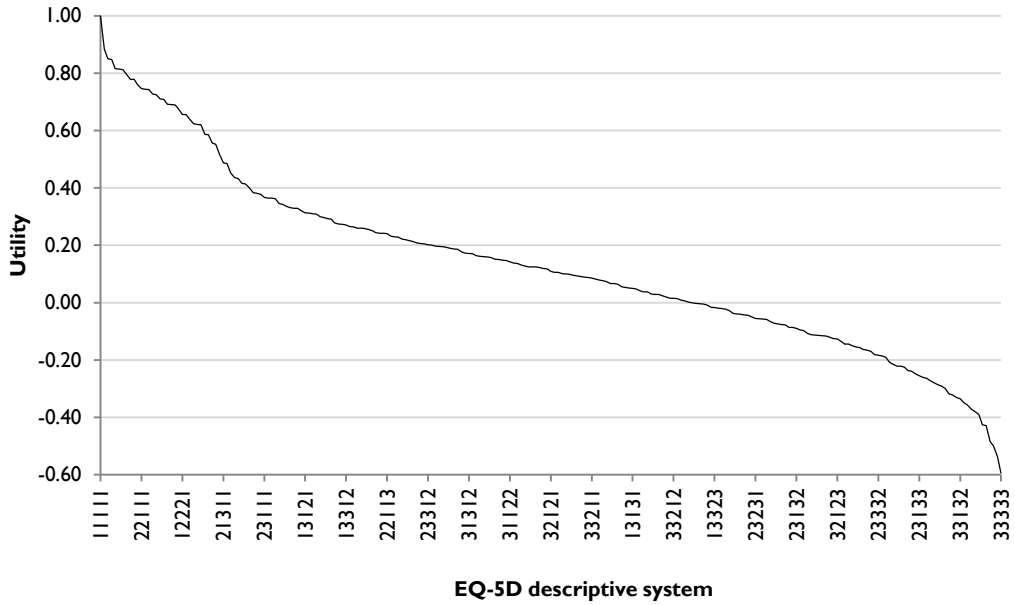

FIGURE 32 - UTILITIES FOR EQ-5D AS VALUED BY UK TTO VALUE SET

A solution to this issue was proposed by Busschbach *et al.*[246] They asserted that a utility set with an upper limit (for example, health state *11111* in the EQ-5D) and a lower limit (that is, health state *33333*) may be calibrated to alternative upper and lower bounds using the values for health states *11111* and *33333* in the alternative set. This may be done using Equation 4.

$$V'(X) = V'(max) - [V(max) - V(X)] \bullet [V'(max) - V'(min)]$$

$V(X)=$	Utility for health state *X* in terms of value set V	$V'(X)=$	Recalibrated utility for health state *X* in terms of value set V'
$V(max)=$	Utility for health state *11111* in terms of value set V	$V'(max)=$	Utility for health state *11111* in terms of value set V'
$V(min)=$	Utility for health state *33333* in terms of value set V	$V'(min)=$	Utility for health state *33333* in terms of value set V'

EQUATION 4- RECALIBRATION OF UTILITIES FROM VALUE SET V TO VALUE SET V' WITH ALTERNATE ANCHOR POINTS FOR BEST AND WORST HEALTH STATES. ADAPTED FROM BUSSCHBACH *ET AL.*[246]

For this study, all GBD, ABDI and Dutch weights were recalibrated to the UK TTO value set using V(*max*)=1.0 and V(*min*)=-0.59 (see Figure 32). These weights were calibrated to the EQ-5D limits rather than vice versa for two reasons:

- the GBD, ADBI and Dutch weights were intended for population-based studies. In contrast, the EQ-5D was designed to measure QOL for individual patients, which was what was being estimated in this study.
- it was anticipated that there would be more utilities derived using the EQ-5D than would be assigned from the GBD, ABDI or Dutch weights. Normalising the minority of utilities to the anchor points of the majority was therefore more appropriate than the converse.

4.2.2.4 Duration of illness

A final consideration in the development of utilities for the consequences related to the duration of adverse effects on QOL. Most of the health states described in the consequences table are single incidents defined by an expected duration. Hence, implicit in Tenni's methodology is the assumption that a patient is in a stable health state until a consequence occurs; their QOL is reduced throughout the duration of the consequence, but returns to its previous level once the consequence resolves. This is

illustrated in Figure 33. In this example, the patient experienced a consequence that reduced their QOL from 0.823 to 0.649 for 29 days in a year, a loss of 0.017 QALYs in that year. An alternative way to express this is that the annualised utility for the consequence is 0.809.

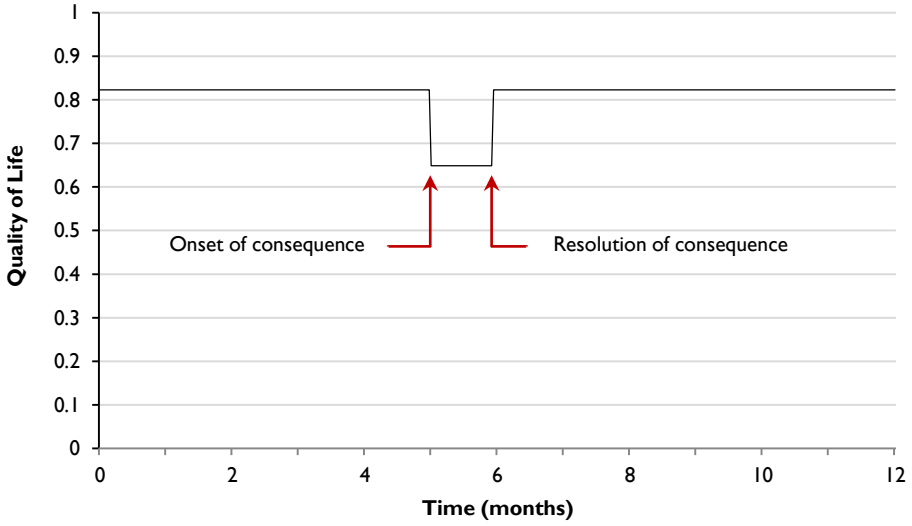

FIGURE 33 - HYPOTHETICAL EXAMPLE ILLUSTRATING QOL BEFORE, DUING AND AFTER A GIVEN HEALTH STATE

The GBD and Dutch weight studies primarily valued chronic diseases, and considered that each health state remained constant throughout one year. Relatively few states were comprised of diseases occurring either in an episodic pattern (for example, an asthma attack) or with a brief duration followed by a full recovery (such as headache or constipation). For episodic conditions, the Dutch weights did not assess attacks; rather, such conditions were described as chronic. The description of the health state included measures to prevent attacks, the side-effects of such measures and the fear of suffering an attack. Brief conditions followed by a full recovery were presented for valuation as an annual profile, for example, one year in good health with the exception of two weeks of influenza during that year. Hence the entire year, and not simply the episode of illness, was presented for assessment.

A potential issue with using this methodology to derive utilities for the consequences table was that many of the consequences were of very limited duration. It was

considered that if the experts assessed the annual profile of a consequence, then many health states may have been valued as having no QOL effect, potentially underestimating the QOL effects of the HMR. To address this issue, the respondents were asked to indicate the expected QOL of a person *currently experiencing the health state* rather than the annual profile of a patient who experiences the health state. To convert these utilities to an annual profile, the estimated duration of each health state (developed in the study described in the previous chapter) was used to indicate the length of time spent in the EQ-5D-derived health state. It was assumed that the patient would spend the remainder of the year in full health. This may be represented by Equation 5.

$$Q_A = \frac{Q \cdot t + (365 - t)}{365}$$

Q_A = annualised utility;
Q = utility while consequence experienced;
t = duration of consequence (days)

EQUATION 5 – CONVERSION OF UTILITIES TO ANNUAL PROFILE

This equation was applied to the utilities sourced from reference sets for consequences of less than 12 months duration and those from the EQ-5D study.

4.2.3 Participants

An important consideration in any study whereby utilities are measured is whose preferences to use. There is significant debate in the literature regarding the most appropriate respondents in such studies, and currently there is no definitive answer.[247] It has been demonstrated that patients and ex-patients adapt to a health state and consequently its effects on QOL are valued as less severe than non-patients.[247] Based on this rationale, both the GBD and Dutch weights were derived using the opinions of health workers.[240, 248]

Following this reasoning, in this study the opinions of physicians were sought to develop utilities using the EQ-5D. To ensure that the participants had a broad, practical knowledge of general medicine, efforts were made to recruit general physicians and clinical pharmacologists. No formal method of recruitment was

applied. The physicians recruited for the VALMER study were invited to participate in this EQ-5D study via personally emailed requests.

4.2.4 Number of assessors

The sample size for this assessment was based on that used in the Dutch Weights study. The Dutch weights used a factorial design whereby each of 45 participants assessed 30 disease stages (out of a possible 153), resulting in each disease stage being assessed by six panel members.[248] As it was anticipated that that the assessment of the health states for this study would not be particularly onerous, a panel of six assessors was recruited, each of whom were to value every level of every consequence.

4.2.5 Data collection

The study was undertaken using questionnaires hosted on an online survey system. Prior to commencing the study, each participant was provided with a manual that outlined the purpose and nature of the assessment (Appendix XVIII). For each health state, respondents were shown the describing vignette for which they then selected the appropriate EQ-5D description from drop-down boxes. An example of the data collection form is shown in Figure 34.

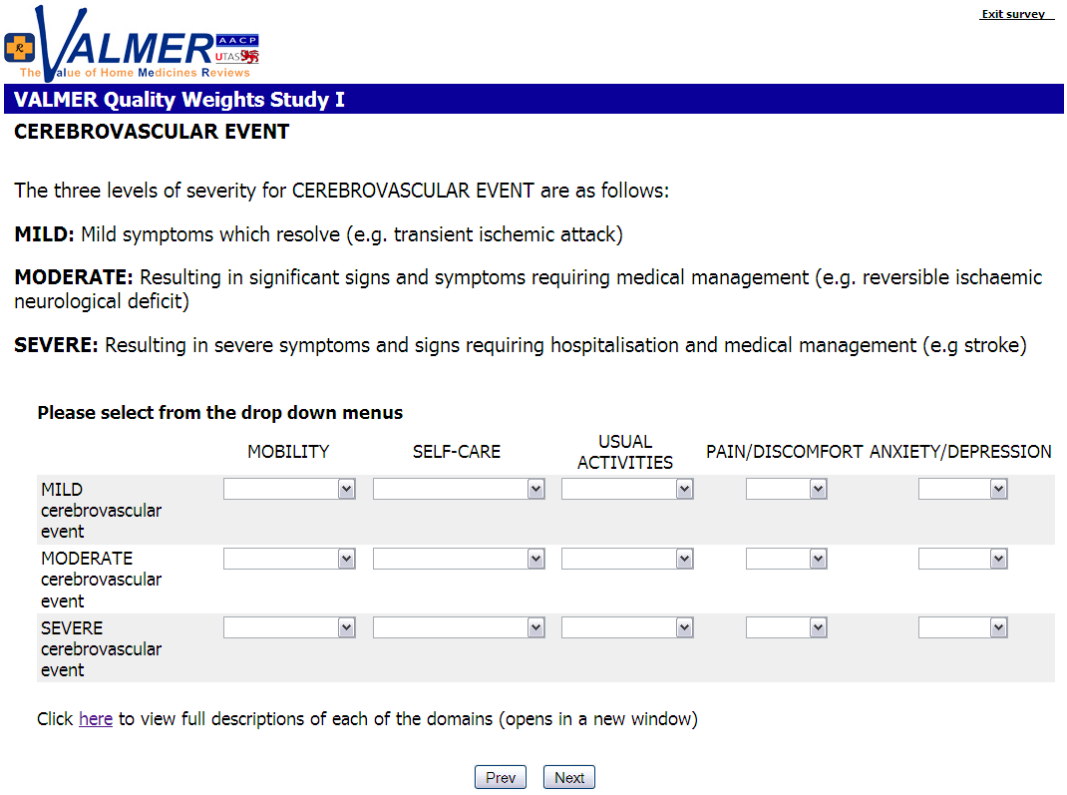

FIGURE 34 - UTILITIES STUDY DATA ENTRY SCREEN

4.2.6 Reliability and validity of the utilities

To ensure robustness of the results of the study, both reliability (consistency between experts) and validity (the degree to which the measurement corresponded to the real world, or previously elucidated values in this case) was assessed. The reliability of the utilities was investigated using Cronbach's α and Fleiss's κ. It was anticipated that the utility assigned to the conditions by the different assessors would not be greatly divergent. However, some variability was expected, since it was unlikely that every assessor would rate each consequence identically. Furthermore, it was envisaged that the variability between the assessors may be used in uncertainty analyses (discussed in Section 2.7).

With regard to validation of the utilities, Stouthard *et al.* asserted that there are no exact criteria to validate utilities.[248] However, they discussed desirable criteria that

should generally be met if the utilities are to be considered reliable. Of those criteria, those relevant to this study were:

- reasonable correlation with the GBD, ABDI and Dutch weights; and
- mutual coherence of the set of weights - that ranking of the disease stages is plausible. For example: intuitively, "minor bleeding" should be valued as less severe than "major bleeding".

Hence, the validity of the utilities measured using the EQ-5D was investigated in two ways. Firstly, the respondents were asked to rate a number of health states for which GBD or Dutch weights were also available. The health states selected for this comparison (Table 41) were selected based on the potential that they would frequently be influenced by the interventions made by pharmacists in HMRs.

TABLE 41 – CONSEQUENCES USED FOR VALIDATION OF UTILITIES

STUDY CONSEQUENCE	SEVERITY LEVEL	REFERENCE FOR COMPARISON
Cerebrovascular event	Mild	DW "Stroke, mild permanent impairments"
	Moderate	DW "Stroke, moderate permanent impairments"
	Severe	DW "Stroke, severe permanent impairments"
Diabetes / hyperglycaemia	Mild	DW "Uncomplicated diabetes mellitus"
Heart failure	Mild	DW "Mild heart failure (NYHA I - 2)"
	Moderate	DW "Moderate heart failure (NYHA 3)"
	Severe	DW "Severe heart failure (NYHA 4)"
Myocardial ischaemia	Mild	DW "Coronary heart disease (excl. heart failure), mild stable angina pectoris (NYHA I-2)"
	Moderate	DW "Coronary heart disease (excl. heart failure), severe stable angina pectoris (NYHA 3)"
	Severe	ABDI "Acute myocardial infarction"
Renal dysfunction	Moderate	GBD "Treated renal failure"
	Severe	DW "Diabetic nephropathy"

ABDI – Australian Burden of Disease and Injury; DW – Dutch Weight
GBD – Global Burden of Disease; NYHA – New York Heart Association

The relationship between the reference set utilities and those derived using the EQ-5D in this study was investigated by calculating correlation coefficients.

To satisfy the need for mutual coherence, the utilities were investigated by consideration of their ranking within each consequence. According to Stouthard *et*

al.,[248] the utilities for any given consequence should be ordered *Mild* > *Moderate* > *Severe*.

4.3 Results

4.3.1 Overview

Tenni's consequences table listed 51 consequences, each at three levels of severity. Consequently, 153 utilities were required from either reference sources or to be measured using the EQ-5D. The reference sets provided utilities for 57 (37%) health states, leaving 96 health states that required measurement of their utility using the EQ-5D. An additional 12 utilities were measured using the EQ-5D for validation purposes (see Table 41), resulting in a total of 108 health states that were evaluated by the experts using the EQ-5D survey.

This is summarised in Table 42.

TABLE 42 – SUMMARY OF SOURCES OF UTILITIES USED IN THE STUDY

SOURCE OF UTILITIES	NUMBER OF HEALTH STATES VALUED		
	UNIQUE	COMMON	TOTAL
REFERENCE SETS	**45**	**12**	**57**
DUTCH WEIGHTS	31	10	41
GLOBAL BURDEN OF DISEASE WEIGHTS	5	1	6
AUSTRALIAN BURDEN OF DISEASE AND INJURY WEIGHTS	9	1	10
DERIVED USING EQ-5D IN THIS STUDY	**96**	**12**	**108**
TOTAL	**141**	**24**	**165**

4.3.2 Utilities assigned from reference sets

The 57 health states for which reference utilities were available are shown in Table 43. Forty-one utilities were sourced from the Dutch weights, and the ABDI weights accounted for ten of the remaining 16 utilities. The column "Unadjusted utility" shows the reference values with upper and lower limits of 1 (full health) and 0 (death) respectively.

However, these unadjusted reference utilities were annualised profiles for each health state. That is, they represented either one year of health living with a chronic condition (50 utilities) or the average health over a year having experienced an episode of an acute illness in that year (7 utilities). As previously discussed, the estimates for the duration of illness for each health state that were developed in the study described in 2.1 of this thesis were considerably less than 12 months. The duration of illness estimates were therefore used to convert the reference utilities to annualised profiles reflecting this study's durations of illness using Equation 5. These annualised profiles were then recalibrated to the EQ-5D upper and lower bounds using Equation 4, and are shown in the column "Recalibrated & annualised utility".

It is notable that these utilities generally satisfy Stouthard's criteria for validity within each consequence. The only exception to this was the unadjusted utilities for the consequence of *myocardial ischaemia*, where the *Moderate* severity level had a greater impact on QOL than the *Severe* level. It is likely that the reason for this is that the *Severe* health state describes a single event, whereas the *Moderate* state describes several episodes of chest pain with limitation of daily activities. This difference was not evident once the utilities had been annualised.

TABLE 43 - UTILITIES ASSIGNED FROM REFERENCE SOURCES

CONSEQUENCE	SEVERITY LEVEL	VIGNETTE	REFERENCE	REFERENCE DESCRIPTION AND RELEVANT NOTES	UTILITY (±SD WHERE AVAILABLE)*	
					UNADJUSTED	RECALIBRATED & ANNUALISED†
Anaemia	Mild	Mild signs or symptoms of anaemia which resolve without intervention. E.g. haemoglobin of 100-109g/L in pregnant women, 110-119g/L in children and adult women, and 120-129g/L in adult men	GBD	Mild anaemia	0.995	1.000
	Moderate	Anaemia requiring medical management and/or modification of medication regimen. E.g. haemoglobin of 70-99g/L in pregnant women, 80-109g/L in children and adult women, and 90-119g/L in adult men	GBD	Moderate anaemia	0.989	0.999
	Severe	Anaemia requiring hospitalisation and blood product or growth factor support. E.g. haemoglobin of 40-69g/L in pregnant women, 50-79g/L in children and adult women, and 60-89g/L in adult men	GBD	Mean of "severe anaemia" and "very severe" anaemia	0.830	0.976
Anxiety	Mild	Mild signs or symptoms of anxiety which resolve without intervention	DW	Mean of "mild-moderate" "agoraphobia", "diffuse anxiety disorder", "obsessive-compulsive disorder", "panic disorder", "post-traumatic stress disorder", "singular phobia" and "social phobia"	0.843 (0.075)	0.989 (0.005)
	Moderate	Worsening of anxiety requiring modification of existing treatment regimen	DW	Mean of "mild-moderate" "agoraphobia", "diffuse anxiety disorder", "obsessive-compulsive disorder", "panic disorder", "post-traumatic stress disorder", "singular phobia" and "social phobia"	0.843 (0.075)	0.975 (0.012)
	Severe	Anxiety requiring specialist medical attention	DW	Mean of "severe" "agoraphobia", "diffuse anxiety disorder", "obsessive-compulsive disorder", "panic disorder", "post-traumatic stress disorder", "singular phobia" and "social phobia"	0.440 (0.215)	0.810 (0.073)

CONSEQUENCE	SEVERITY LEVEL	VIGNETTE	REFERENCE	REFERENCE DESCRIPTION AND RELEVANT NOTES	UTILITY (±SD WHERE AVAILABLE)*	
					UNADJUSTED	RECALIBRATED & ANNUALISED†
Bleeding, non-specific	Mild	Easy bruising, bleeding from small cuts, petechia, ecchymosis, mild elevation of INR not requiring adjustment of dosage	ABDI	Mild cases of haemophilia not valued	1.000	1.000
	Moderate	Haematoma, epistaxis, blood loss from mouth, vagina, melaena, eye bleed, haematuria, haematemesis, moderate elevation of INR requiring modification of dose of anticoagulant	ABDI	Moderate cases of haemophilia	0.950	0.998
	Severe	Severe bleeding requiring hospitalisation, blood product and/or haemodynamic support	ABDI	Severe cases of haemophilia	0.730	0.974
Cerebrovascular event	Mild	Mild symptoms which resolve (e.g. transient ischemic attack)	DW	Stroke - mild permanent impairments	0.640 (0.064)	0.994 (0.001)
	Moderate	Resulting in significant signs and symptoms requiring medical management (e.g. reversible ischaemic neurological deficit)	DW	Stroke - moderate permanent impairments	0.370 (0.045)	0.972 (0.002)
	Severe	Resulting in severe symptoms and signs requiring hospitalisation and medical management (e.g stroke)	DW	Stroke - severe permanent impairments	0.080 (0.038)	0.574 (0.017)
Chronic airways disease	Mild	Mild chronic airways disease which does not require medical intervention	DW	Mild to moderate COPD/ asthma (symptom-free with or without maintenance therapy)	0.970 (0.010)	0.993 (0.000)
	Moderate	Chronic airways disease requiring medical intervention and/or modification of medication	DW	Mild to moderate COPD/ asthma	0.830 (0.051)	0.985 (0.004)
	Severe	Severe chronic airways disease requiring hospitalisation and medical intervention	DW	Severe COPD	0.470 (0.078)	0.862 (0.020)
Dementia	Mild	Dementia resulting in some impairment of daily activities only	DW	Mild dementia (only significant impairment of daily activities)	0.730 (0.076)	0.928 (0.020)

CONSEQUENCE	SEVERITY LEVEL	VIGNETTE	REFERENCE	REFERENCE DESCRIPTION AND RELEVANT NOTES	UTILITY (±SD WHERE AVAILABLE)*	
					UNADJUSTED	RECALIBRATED & ANNUALISED†
	Moderate	Dementia to the extent that independent living is not possible without limited supervision	DW	Moderate dementia (independent living is not possible without limited supervision)	0.370 (0.115)	0.606 (0.004)
	Severe	Dementia to the extent that permanent supervision is required	DW	Severe dementia (permanent supervision required)	0.060 (0.007)	0.111 (0.026)
Depression	Mild	Mild signs or symptoms of depression which resolve without intervention	DW	Mild depression	0.860 (0.028)	0.994 (0.002)
	Moderate	Worsening of depression requiring modification of treatment regimen	DW	Moderate depression	0.650 (0.038)	0.963 (0.011)
	Severe	Destabilisation or unmasking of depression requiring specialist medical attention	DW	Severe depression	0.205 (0.108)	0.724 (0.004)
Diabetes/ hyperglycaemia	Mild	Reduced control of diabetes requiring increased monitoring	DW	Uncomplicated diabetes	0.930 (0.012)	0.998 (0.000)
Diarrhoea	Mild	Mild signs or symptoms of diarrhoea likely to resolve without intervention	DW	Digestive tract infection, uncomplicated course (duration 2 weeks)	0.990 (0.000)	0.997 (0.001)
	Moderate	Diarrhoea requiring medical management and/or modification of medication	DW	Digestive tract infection, complicated course (duration 2 weeks)	0.970 (0.005)	0.972 (0.045)
	Severe	Requiring hospitalisation for significant diarrhoea-related electrolyte and hydration complications	DW	Acute exacerbation of inflammatory bowel disease	0.600 (0.048)	0.974 (0.000)
Glaucoma	Mild	Mild elevation of IOP not requiring intervention	DW	Mild vision loss	0.980 (0.007)	1.000 (0.001)
	Moderate	Moderate elevation of IOP requiring medical intervention	DW	Moderate vision loss	0.830 (0.055)	0.982 (0.005)
	Severe	Severe glaucoma requiring acute medical or surgical intervention	DW	Severe vision loss	0.570 (0.046)	0.887 (0.002)

CONSEQUENCE	SEVERITY LEVEL	VIGNETTE	REFERENCE	REFERENCE DESCRIPTION AND RELEVANT NOTES	UTILITY (±SD WHERE AVAILABLE)*	
					UNADJUSTED	RECALIBRATED & ANNUALISED†
Heart failure	Mild	Mild signs or symptoms of heart failure (e.g NYHA class II) which resolve without intervention	DW	Heart failure - mild (NYHA 1 - 2)	0.940 (0.010)	0.991 (0.012)
	Moderate	Resulting in significant signs and symptoms of heart failure (e.g. NYHA class III) requiring medical management by modification of medication regimen	DW	Heart failure - moderate (NYHA 3)	0.650 (0.086)	0.925 (0.006)
	Severe	Significant signs and symptoms of heart failure (e.g. NYHA class IV) requiring hospitalisation and medical management (e.g. acute pulmonary oedema)	DW	Heart failure - severe (NYHA 4)	0.350 (0.028)	0.681 (0.004)
Infection, general	Mild	Mild signs or symptoms of infection which resolve without intervention	DW	Acute bronchitis (duration 2 weeks, 1 episode a year)	0.990 (0.009)	0.996 (0.016)
	Moderate	Infection with moderate complications requiring medical attention and oral antibiotics (e.g. PSI class I pneumonia)	DW	Pneumonia, acute bronchitis and bronchiolitis - pneumonia (duration 2 weeks)	0.900 (0.046)	0.888 (0.031)
	Severe	Infection requiring hospitalisation and intravenous antibiotics (eg PSI class III pneumonia)	DW	Influenza (duration 2 weeks)	0.840 (0.028)	0.590 (0.036)
Myocardial ischaemia	Mild	Mild signs or symptoms of angina (e.g. NYHA class I to II) which resolve without intervention	DW	Coronary heart disease (excl heart failure) - mild stable angina pectoris (NYHA 1-2)	0.920 (0.014)	0.998 (0.002)
	Moderate	Moderate myocardial ischaemia resulting in significant signs and symptoms requiring medical management by modification of medication regimen (e.g. worsened stable angina)	DW	Coronary heart disease (excl heart failure) - severe stable angina pectoris (NYHA 3)	0.430 (0.076)	0.967
	Severe	Myocardial ischaemia resulting in severe symptoms and signs requiring hospitalisation and medical management (e.g unstable angina, myocardial infarction)	ABDI	Acute myocardial infarction (treated)	0.605	0.931
Osteoporosis	Mild	Worsening of osteoporosis requiring increased monitoring	GBD	Osteoporosis – diagnosed cases	0.991	0.999

CONSEQUENCE	SEVERITY LEVEL	VIGNETTE	REFERENCE	REFERENCE DESCRIPTION AND RELEVANT NOTES	UTILITY (±SD WHERE AVAILABLE)*	
					UNADJUSTED	RECALIBRATED & ANNUALISED†
	Moderate	Osteoporosis requiring modification of existing treatment regimen, or commencing treatment for an "at risk" person	GBD	Osteoporosis – diagnosed cases	0.991	0.998
	Severe	Osteoporosis resulting in hospitalisation due to a major complication (e.g. fracture)	DW	Mean of "permanent impairments after fracture of" "arm or shoulder", "hip or leg" and "ankle", and "hip fracture during rehabilitation"	0.897 (0.076)	0.962 (0.028)
Parkinsonism	Mild	Mild Parkinsonian symptoms of tremors and rigidity; slowness, impaired swallowing and speech; disturbance of equilibrium; patient is able to function independently	DW	M. Parkinson initial stage (initially unilateral, later bilateral tremors and rigidity; slowness, impaired swallowing and speech; disturbance of equilibrium; patient are able to function independently)	0.520 (0.081)	0.920 (0.014)
	Moderate	Swallowing and speech severely impaired; autonomic nervous system disturbances; patients are ADL-dependent, but are able to move without help	DW	M. Parkinson intermediate stage (swallowing and speech severely impaired; autonomic nervous system disturbances; patients are ADL-dependent, but are able to move without help)	0.210 (0.035)	0.714 (0.013)
	Severe	Severe Parkinsonian symptoms- patient wheelchair and bed-bound; severely handicapped	DW	M. Parkinson end-stage (wheelchair and bed patient, severely handicapped)	0.080 (0.015)	0.195 (0.013)
Psychosis	Mild	Mild signs or symptoms of psychosis which resolve without intervention	DW	One psychotic episode, no permanent impairments	0.790 (0.072)	0.992 (0.003)
	Moderate	Worsening of psychotic illness requiring modification of treatment regimen	DW	Several psychotic episodes, some permanent impairment	0.290 (0.040)	0.866 (0.007)
	Severe	Destabilisation or unmasking of psychosis requiring specialist medical attention	DW	Several psychotic episodes, obvious permanent impairments	0.190 (0.046)	0.676 (0.019)
Renal dysfunction	Moderate	Renal dysfunction requiring medical management and/or modification of medication regimen	GBD	Treated renal failure	0.890	0.997
	Severe	Acute decline in renal function requiring prompt medical management and investigation	DW	Diabetic nephropathy; used by ABDI for "end stage renal failure"	0.710 (0.046)	0.947 (0.008)

CONSEQUENCE	SEVERITY LEVEL	VIGNETTE	REFERENCE	REFERENCE DESCRIPTION AND RELEVANT NOTES	UTILITY (±SD WHERE AVAILABLE)*	
					UNADJUSTED	RECALIBRATED & ANNUALISED†
Urinary incontinence	Mild	Mild signs or symptoms of urinary incontinence which resolve without intervention	ABDI	Occasional urine leakage	1.000	1.000
	Moderate	Urinary incontinence requiring medical management and/or modification of medication regimen	ABDI	Moderate incontinence	0.975	0.997
	Severe	Urinary incontinence requiring hospitalisation and medical and/or surgical management	ABDI	Severe incontinence	0.843	0.931
Urinary retention	Mild	Symptomatic urinary retention not requiring medical management	ABDI	Symptomatic benign prostatic hypertrophy	0.972	1.000
	Moderate	Symptomatic urinary retention requiring medical management	ABDI	Urethral stricture associated with benign prostatic hypertrophy	0.849	0.995
	Severe	Symptomatic urinary retention requiring catheterisation	ABDI	Urinary incontinence associated with benign prostatic hypertrophy	0.843	0.985
Urinary Tract Infection	Mild	Mild signs or symptoms of UTI which resolve without intervention	DW	Acute non-STI urethritis (duration 1 week)	0.990 (0.007)	0.996 (0.003)
	Moderate	Moderate UTI requiring medical attention and oral antibiotics	DW	Acute cystitis (duration 1 week)	0.990 (0.014)	0.991 (0.013)
	Severe	UTI requiring hospitalisation and intravenous antibiotics, e.g. pyelonephritis	DW	Acute pyelitis/ pyelonephritis (duration 2 weeks)	0.990 (0.007)	0.987 (0.009)

ABDI – Australian Burden of Disease and Injury; DW – Dutch Weight; GBD – Global Burden of Disease
* Converted from disability weight – see Equation 2. SD unavailable for GBD and ABDI utilities
† Recalibrated to UK TTO EQ-5D bounds (Equation 4) and annualised using Equation 5

4.3.3 Utilities developed using EQ-5D

Utilities for the remaining health states were assessed by the recruited experts during a five-week period between February and March 2009. Each expert who commenced the study completed it, resulting in six opinions being obtained for each of the 108 health states.

4.3.3.1 Characteristics of the experts

The six experts were all specialist physicians actively practicing in Australian hospitals. Their specialties and state of practice are shown in Table 44. Aside from the Western Australian physician who worked in a regional centre, all experts practised in capital cities.

TABLE 44 - GENERAL DEMOGRAPHICS OF EXPERTS WHO PARTICIPATED IN THE UTILITIES STUDY

EXPERT	STATE OF PRACTICE	SPECIALTY
One	Tasmania	Respiratory and general medicine
Two	South Australia	Endocrinology
Three	Western Australia	General medicine
Four	Tasmania	General medicine
Five	Tasmania	Endocrinology
Six	Tasmania	Rheumatology and general medicine

The mean time for the experts to perform the assessment was 55 minutes (st dev 28 minutes, range 30 to 106 minutes).

4.3.3.2 Initial utility estimates

Descriptive statistics for the results of this section of the study are shown in Table 45. In this table, the EQ-5D responses have been mapped to utilities using the UK TTO value set (Equation 3) but have not been converted to the annual profile.

Several of the consequences relating to biochemical abnormalities (e.g. hyperkalaemia and acidosis) were considered to not adversely affect QOL at mild severity levels, potentially due to them being relatively asymptomatic. However, as the severity level

increased, their adverse effects on QOL were considerable. In contrast, the utilities for consequences with overt symptoms at even mild severity levels (such as nausea, heart failure and cerebrovascular events) indicated a substantial impact on QOL, which was to be expected as, intuitively, a symptomatic condition is more likely to affect QOL than an asymptomatic one.

TABLE 45 - UTILITIES DERIVED FROM EXPERT OPINION VIA EQ-5D RESPONSES MAPPED TO UK TTO VALUE SET (ESTIMATED QOL WHILST EXPERIENCING CONSEQUENCE)

CONSEQUENCE	MEAN UTILITY (SD) [RANGE] AT SEVERITY LEVEL (N=6)		
	MILD	MODERATE	SEVERE
Acidosis	1.000 (0.000) [1.000 to 1.000]	0.812 (0.103) [0.689 to 1.000]	0.130 (0.342) [-0.331 to 0.516]
Alkalosis	0.929 (0.117) [0.725 to 1.000]	0.903 (0.124) [0.689 to 1.000]	0.378 (0.367) [-0.166 to 0.743]
Allergic reaction	0.839 (0.082) [0.796 to 1.000]	0.655 (0.076) [0.516 to 0.725]	-0.219 (0.430) [-0.594 to 0.516]
Arrhythmia	0.722 (0.095) [0.620 to 0.848]	0.478 (0.228) [0.189 to 0.689]	-0.173 (0.351) [-0.594 to 0.293]
Asthma	0.779 (0.197) [0.516 to 1.000]	0.597 (0.068) [0.516 to 0.689]	-0.358 (0.260) [-0.594 to 0.079]
Bone marrow suppression	0.873 (0.116) [0.691 to 1.000]	0.698 (0.197) [0.516 to 1.000]	0.371 (0.439) [-0.331 to 0.812]
Cerebrovascular event	0.697 (0.151) [0.516 to 0.848]	0.461 (0.320) [-0.166 to 0.743]	-0.052 (0.147) [-0.221 to 0.082]
Central nervous system depression	0.609 (0.125) [0.516 to 0.812]	0.275 (0.276) [-0.108 to 0.516]	-0.320 (0.230) [-0.594 to -0.095]
Confusion	0.698 (0.072) [0.639 to 0.812]	0.528 (0.185) [0.202 to 0.708]	0.061 (0.159) [-0.166 to 0.202]
Constipation	0.795 (0.107) [0.725 to 1.000]	0.725 (0.000) [0.725 to 0.725]	0.216 (0.407) [-0.181 to 0.725]
Diabetes	0.918 (0.091) [0.812 to 1.000]	0.826 (0.102) [0.725 to 1.000]	0.609 (0.089) [0.516 to 0.689]
Gastrointestinal bleeding	0.975 (0.062) [0.848 to 1.000]	0.592 (0.228) [0.189 to 0.848]	-0.197 (0.249) [-0.594 to 0.189]
Gastrointestinal pain	0.719 (0.042) [0.689 to 0.796]	0.620 (0.085) [0.516 to 0.689]	-0.430 (0.222) [-0.594 to -0.074]
Headache	0.806 (0.101) [0.725 to 1.000]	0.696 (0.068) [0.585 to 0.796]	-0.279 (0.271) [-0.594 to 0.088]
Heart failure	0.705 (0.134) [0.516 to 0.883]	0.436 (0.125) [0.258 to 0.516]	-0.380 (0.188) [-0.594 to -0.056]
Hypercalcaemia	0.966 (0.083) [0.796 to 1.000]	0.858 (0.122) [0.689 to 1.000]	0.324 (0.337) [-0.208 to 0.743]
Hyperkalaemia	1.000 (0.000) [1.000 to 1.000]	1.000 (0.000) [1.000 to 1.000]	0.515 (0.297) [0.048 to 0.883]
Hypertension	1.000 (0.000) [1.000 to 1.000]	0.975 (0.062) [0.848 to 1.000]	0.459 (0.397) [-0.331 to 0.725]

Consequence	Mean utility (SD) [range] at severity level (n=6)		
	Mild	Moderate	Severe
Hyperthyroidism	0.949 (0.078) [0.848 to 1.000]	0.840 (0.241) [0.378 to 1.000]	0.482 (0.221) [0.205 to 0.725]
Hypocalcaemia	0.954 (0.112) [0.725 to 1.000]	0.826 (0.157) [0.621 to 1.000]	0.311 (0.459) [-0.331 to 0.812]
Hypoglycaemia	0.835 (0.092) [0.743 to 1.000]	0.757 (0.156) [0.620 to 1.000]	0.039 (0.272) [-0.208 to 0.516]
Hypokalaemia	1.000 (0.000) [1.000 to 1.000]	0.894 (0.195) [0.516 to 1.000]	0.274 (0.496) [-0.594 to 0.639]
Hypotension	0.815 (0.121) [0.620 to 1.000]	0.694 (0.142) [0.516 to 0.883]	-0.226 (0.215) [-0.594 to 0.002]
Hypothyroidism	0.975 (0.062) [0.848 to 1.000]	0.924 (0.086) [0.812 to 1.000]	0.564 (0.247) [0.189 to 0.812]
Insomnia	0.867 (0.067) [0.812 to 1.000]	0.716 (0.203) [0.378 to 1.000]	0.516 (0.174) [0.274 to 0.725]
Liver disease	0.892 (0.130) [0.689 to 1.000]	0.707 (0.183) [0.516 to 1.000]	0.179 (0.443) [-0.594 to 0.689]
Myocardial ischaemia	0.591 (0.086) [0.516 to 0.691]	0.478 (0.201) [0.082 to 0.620]	-0.275 (0.269) [-0.484 to 0.189]
Myopathy	0.720 (0.087) [0.620 to 0.796]	0.598 (0.079) [0.516 to 0.727]	-0.083 (0.434) [-0.594 to 0.620]
Nausea	0.731 (0.076) [0.620 to 0.796]	0.589 (0.201) [0.258 to 0.796]	-0.207 (0.348) [-0.594 to 0.186]
Oedema	0.885 (0.198) [0.516 to 1.000]	0.661 (0.081) [0.516 to 0.727]	0.225 (0.240) [-0.056 to 0.516]
Pain	0.690 (0.089) [0.585 to 0.796]	0.483 (0.369) [-0.239 to 0.796]	-0.317 (0.204) [-0.594 to -0.016]
Rash	0.765 (0.139) [0.585 to 1.000]	0.696 (0.103) [0.516 to 0.796]	0.016 (0.394) [-0.349 to 0.725]
Renal dysfunction	0.954 (0.112) [0.725 to 1.000]	0.894 (0.195) [0.516 to 1.000]	0.500 (0.366) [-0.208 to 0.812]
Respiratory depression	0.725 (0.115) [0.585 to 0.883]	0.517 (0.184) [0.189 to 0.743]	-0.273 (0.122) [-0.429 to -0.086]
Seizures	0.600 (0.321) [-0.043 to 0.848]	0.392 (0.314) [-0.043 to 0.812]	-0.249 (0.224) [-0.594 to 0.024]
Serotonin toxicity	0.699 (0.326) [0.082 to 1.000]	0.411 (0.461) [-0.484 to 0.812]	-0.200 (0.264) [-0.594 to 0.186]

4.3.3.3 Annualised utility estimates

The experts' EQ-5D responses were based on their estimates of a patient's QOL when they were experiencing the health state. However, each of the estimates for the duration of illness for each health state that were developed in the study described in 2.1 of this thesis were considerably less than 12 months. The consequences table was developed to represent the cost incurred and QOL loss resulting from each health state for a time horizon of 12 months; therefore, the duration of illness estimates were used to convert the experts' EQ-5D responses to annualised utilities using Equation 5.

Descriptive statistics for the annualised utilities are shown in Table 46.

TABLE 46 - ANNUALISED UTILITIES DERIVED FROM EXPERT OPINION VIA EQ-5D RESPONSES MAPPED TO UK TTO VALUE SET

CONSEQUENCE	MILD		MODERATE		SEVERE	
	MEAN DURATION*	MEAN (SD) UTILITY	MEAN DURATION*	MEAN (SD) UTILITY	MEAN DURATION*	MEAN (SD) UTILITY
Acidosis	8.9	1.000 (0.000)	11.4	0.973 (0.003)	22.5	0.938 (0.021)
Alkalosis	9.4	0.998 (0.003)	8.5	0.986 (0.003)	17.6	0.952 (0.018)
Allergic reaction	1.5	0.999 (0.000)	3.8	0.987 (0.001)	8.4	0.977 (0.010)
Arrhythmia	8.1	0.994 (0.002)	21.6	0.931 (0.013)	40.1	0.890 (0.039)
Asthma	6.9	0.996 (0.004)	13.6	0.949 (0.003)	37.1	0.898 (0.026)
Bone marrow suppression	6.6	0.998 (0.002)	18.1	0.969 (0.010)	51	0.860 (0.061)
Cerebrovascular event	3.9	0.997 (0.002)	10.1	0.971 (0.009)	106.2	0.709 (0.043)
Central nervous system depression	8.2	0.991 (0.003)	29.1	0.895 (0.022)	83.2	0.772 (0.052)
Confusion	5.2	0.996 (0.001)	17.8	0.954 (0.009)	62.5	0.829 (0.027)
Constipation	6.1	0.997 (0.002)	11.7	0.975 (0.000)	22.6	0.938 (0.025)
Diabetes	5.8	0.999 (0.001)	10.8	0.988 (0.003)	41.5	0.886 (0.010)
Gastrointestinal bleeding	1.9	1.000 (0.000)	8.8	0.971 (0.005)	31.7	0.913 (0.022)
Gastrointestinal pain	9.9	0.992 (0.001)	11.2	0.956 (0.003)	27.6	0.924 (0.017)
Headache	4.9	0.997 (0.001)	8.4	0.971 (0.002)	17.2	0.953 (0.013)
Heart failure	33.1	0.973 (0.012)	49.4	0.813 (0.017)	112.6	0.692 (0.058)
Hypercalcaemia	4	1.000 (0.001)	10.6	0.980 (0.004)	26.4	0.928 (0.024)
Hyperkalaemia	2.7	1.000 (0.000)	7.9	0.990 (0.000)	18.9	0.948 (0.015)
Hypertension	1.9	1.000 (0.000)	6.5	0.990 (0.001)	32.8	0.910 (0.036)

Consequence	Mild		Moderate		Severe	
	Mean duration*	Mean (SD) utility	Mean duration*	Mean (SD) utility	Mean duration*	Mean (SD) utility
Hyperthyroidism	5.1	0.999 (0.001)	12.5	0.982 (0.008)	32.4	0.911 (0.020)
Hypocalcaemia	3.7	1.000 (0.001)	9.4	0.982 (0.004)	24.5	0.933 (0.031)
Hypoglycaemia	3.8	0.998 (0.001)	8.1	0.979 (0.003)	14.4	0.961 (0.011)
Hypokalaemia	3.6	1.000 (0.000)	10.3	0.980 (0.006)	27.4	0.925 (0.037)
Hypotension	4.1	0.998 (0.001)	9.9	0.967 (0.004)	21.2	0.942 (0.012)
Hypothyroidism	8.8	0.999 (0.001)	14.7	0.982 (0.003)	27.1	0.926 (0.018)
Insomnia	8.3	0.997 (0.002)	16.6	0.978 (0.009)	29	0.921 (0.014)
Liver disease	4.4	0.999 (0.002)	12.7	0.971 (0.006)	48.2	0.868 (0.059)
Myocardial ischaemia	6.1	0.993 (0.001)	13.1	0.954 (0.007)	40.3	0.890 (0.030)
Myopathy	9.1	0.993 (0.002)	13	0.961 (0.003)	18.3	0.950 (0.022)
Nausea	3.2	0.998 (0.001)	6.4	0.979 (0.004)	13.1	0.964 (0.012)
Oedema	4	0.999 (0.002)	9.8	0.979 (0.002)	37.9	0.896 (0.025)
Pain	6.8	0.994 (0.002)	13.9	0.950 (0.014)	71.7	0.804 (0.040)
Rash	3.1	0.998 (0.001)	11.9	0.968 (0.003)	48.2	0.868 (0.052)
Renal dysfunction	1.4	1.000 (0.000)	7.2	0.990 (0.004)	41.6	0.886 (0.042)
Respiratory depression	3.4	0.997 (0.001)	11.9	0.958 (0.006)	48.7	0.867 (0.016)
Seizures	2.4	0.997 (0.002)	6	0.979 (0.005)	29.2	0.920 (0.018)
Serotonin toxicity	3.7	0.997 (0.003)	9.4	0.969 (0.012)	15.2	0.958 (0.011)

*Duration in days

4.3.3.4 Reliability and validity of the utilities

4.3.3.4.1 Reliability

The reliability between the experts was assessed using each expert's responses to the EQ-5D descriptive system (i.e. categorical data). The results from the assessment of utilities for the 108 consequences was initially analysed by calculating Cronbach's α. It is generally considered that a minimum Cronbach's α of between 0.7 and 0.8 indicates acceptable reliability between subjects.[221] For the utility study, Cronbach's α was calculated to be 0.984, indicating a very high level of reliability.

Cronbach's α is sensitive to the number of items in the assessment, and may be inflated as a result of many items on a scale rather than the scale itself being reliable.[221] For this application, there were 540 items (5 EQ-5D domains for the 108 severity levels of the consequences were rated by each assessor). To further investigate the reliability of the responses, Fleiss' κ was also calculated. Fleiss' κ is a measure for assessing the reliability of agreement between a fixed number of raters when assigning categorical ratings to a number of items.[249] Fleiss' κ is frequently interpreted according to the parameters shown in Table 47, although these divisions are arbitrary and not grounded in statistical theory.[250] In contrast to Cronbach's α, Fleiss' κ tends to be higher when there are fewer categories.[251]

TABLE 47 - INTERPRETATION OF Κ STATISTICS. REPRODUCED FROM LANDIS AND KOCH[250]

FLEISS' Κ STATISTIC	STRENGTH OF AGREEMENT
<0.00	Poor
0.00 - 0.20	Slight
0.21 - 0.40	Fair
0.41 – 0.60	Moderate
0.61 – 0.80	Substantial
0.81 – 1.00	Almost perfect

The test returned a value of κ=0.433, indicating moderate agreement between the assessors.

Based on the results of this analysis, it was concluded with a moderate level of confidence that the utilities were reliable. Nonetheless, the results of this analysis illustrate that there was some uncertainty regarding their true value, and it was concluded that uncertainty analysis should be undertaken when the values were to be used, to account for this.

4.3.3.4.2 Validity

As discussed in Section 4.2.6 of this chapter, 12 health states with literature utilities were also valued by the experts to assess the validity of the EQ-5D assessment. A comparison between the utilities derived using the EQ-5D and literature values for these 12 health states is shown in Table 48.

TABLE 48 - COMPARISON BETWEEN REFERENCE UTILITIES AND THOSE MEASURED USING EQ-5D (ANNUALISED ESTIMATES)

CONSEQUENCE	SEVERITY LEVEL	MEAN UTILITY (SD)	
		RECALIBRATED REFERENCE	DERIVED USING EQ-5D
Cerebrovascular event	Mild	0.994 (0.001)	0.997 (0.002)
	Moderate	0.972 (0.002)	0.971 (0.009)
	Severe	0.574 (0.017)	0.709 (0.043)
Diabetes / hyperglycaemia	Mild	0.998 (0.000)	0.999 (0.001)
Heart failure	Mild	0.991 (0.012)	0.973 (0.012)
	Moderate	0.925 (0.006)	0.813 (0.017)
	Severe	0.681 (0.004)	0.692 (0.058)
Myocardial ischaemia	Mild	0.998 (0.002)	0.993 (0.001)
	Moderate	0.967	0.954 (0.007)
	Severe	0.931	0.890 (0.030)
Renal dysfunction	Moderate	0.997	0.990 (0.004)
	Severe	0.947 (0.008)	0.886 (0.042)

Whilst differences between the utilities were apparent, neither utility set consistently valued the consequences higher than the other. The greatest discrepancies primarily involved the consequences at higher severity levels, which appears consistent with the results reported by Mathers *et al.*[242]

The relationship between the different utilities was investigated using the Pearson product-moment correlation coefficient and Kendall's non-parametric test. The Pearson product-moment correlation indicated that there was a strong positive correlation between the two utilities (r=0.92, n=12, P<0.001), which was consistent with the correlation coefficient of 0.91 reported by Mathers *et al.* (Figure 30, page 171).[242] Kendall's non-parametric test also indicated significant correlation between the two sets of utilities (tau-b value=0.87, P<0.001).

The relationship between the utilities is illustrated in Figure 35.

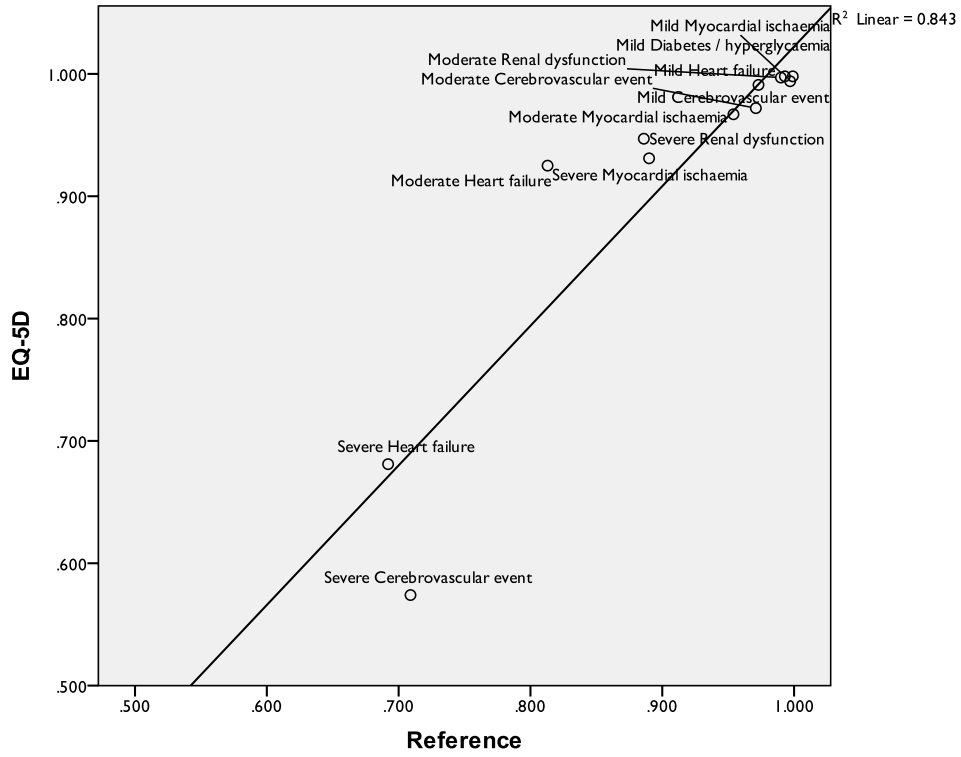

FIGURE 35 - SCATTERPLOT ILLUSTRATING CORRELATION BETWEEN REFERENCE UTILITIES AND THOSE MEASURED USING EQ-5D

The QOL impact of the health states *Severe* heart failure and *Severe* cerebrovascular event were substantially greater than the other utilities in this analysis. However, removal of these two health states from the analysis did not appreciably alter the correlation between the utility sets (Pearson product-moment correlation r=0.95, n=10, P<0.001; Kendall's non-parametric test tau-b value=0.85, P=0.001).

4.3.4 Distributions fitted

With regards to the consequences for which reference weights were used, Stouthard *et al.* provided 95% confidence intervals for their disability weights.[248] It was assumed that the uncertainty of these weights was normally distributed, so the confidence intervals were used to define the standard deviation for each utility which was then assigned a beta distribution. Uncertainty for the utilities developed from the EQ-5D was determined using the best-fit function included in the software program @RISK. This program attempts to find the best parameters for a distribution around a given set of raw data, as discussed in Section 2.6.4. There was total agreement between the experts for nine of the health states and hence no distribution was fitted to these health states. The @Risk program determined best-fit beta distributions for each of the remaining 99 health states; no degenerate distributions required calculation.

The distributions and the parameters describing them for each health state are shown in the complete consequences table (Appendix XVII).

4.4 Discussion

The primary aim of the research undertaken in this study was to develop utilities for each of the health states in the consequences table. The aim of the study was achieved, with the results shown to have reasonable internal consistency (reliability) and be comparable with those of previous studies (validity). It was envisaged that the results of this research would add the additional outcome measure of QOL to the results of economic analyses performed using Tenni's methodology, allowing CUA to be undertaken.

Two approaches were used to develop the utilities for the health states in this study, namely reference sets and the EQ-5D. It may be argued that this approach may have resulted in the results being less valid than had a single method been used for each health state, as it has been reported that utilities derived from one technique often do not directly equate to utilities obtained using an alternate technique.[231, 232, 237] Consequently, a more robust method may have been to value every health state using the same approach; however, the strength of the correlation between the reference and measured utilities implies that this is unlikely to have greatly confounded the

results. By initially using literature values where possible, the number of health states that required measurement using the EQ-5D was substantially reduced. This resulted in reduced costs of the study, and consequently a greater number of experts were involved in valuing the remaining health states using the EQ-5D.

The opinion of experts was used to elicit utilities for health states for which reference values were unavailable. Whilst it may be argued that using the opinion of patients may be more appropriate,[247] utilities developed from expert opinion such as clinicians have frequently been used in previous studies. In their analysis of 88 studies that estimated QALYs, Neumann *et al*. found that 62% of the studies used responses from either clinicians or authors.[252] More recently, a review of 1000 conditions by Tengs and Wallace reported that 54% of health states were valued by clinicians or authors.[232] Similarly, Bell *et al*. found that 60.9% of 949 health states were estimated by clinicians or authors analysed in 228 CUAs.[231] It therefore seems unlikely that the use of expert opinion would have adversely affected the validity of the results of this new study in contrast to previous research. However, the question as to how well the estimates approximate patients' experiences remains a limitation of the study. A potential resolution to this issue may be to develop a second set of utilities based on patient responses and use this in a one-way sensitivity analysis in subsequent economic evaluations. However, it is likely that there would be significant costs and time required to undertake such a study. Furthermore, the value of this additional analysis is debatable, given the quantity of literature that has relied upon utilities derived using expert opinion.

The choice of reference utilities and the use of the EQ-5D to value the health states in this new study overcame a methodological issue present in many previous studies. The reviews by Neumann *et al*., Bell *et al*. and Tengs and Wallace reported that many studies have not used recognised methods to elicit utilities. Neumann *et al*. found that simple judgement was used to value 38% of the health states included in their review.[252] Similar findings were reported by both Tengs and Wallace (32%) and Bell *et al*. (32.5%).[231, 232] By not using a formal measurement technique and relying upon simple judgement, there is the potential for arbitrariness to adversely affect the robustness of the results.[232] The utilities in the Dutch Weights, GBD and ABDI studies were all developed using robust methodology.[240-242] Similarly, the EQ-5D was used to value the remaining health states in this new study, which is recognised as a valid

methodology for QOL measurement.[235] Consequently, the utilities may be considered to be more robust than those reported in many previous studies. Further evidence of the robustness of the results is that there was reasonable reliability, which suggests that they are plausible estimates of the QOL of patients experiencing the health states.

Despite these strengths, there are limitations to this research that must be acknowledged. Perhaps most importantly is that the utilities are generalisations; that is, they are representative of the average QOL effect of each health state. As a consequence, patients who experience a greater or lesser QOL loss from a health state (which is often the case due to factors such as age, co-morbidity and race)[232] will not be accurately represented. The study sought to overcome this limitation by using PSA to represent the utilities instead of simple averages; however, this only captured inter-rater variation, rather than intra-rater. Additionally, for several health states there was 100% agreement between the experts or no confidence interval reported in the reference, so no distribution could be assigned. As discussed in the previous chapter, some authors have investigated measuring experts' estimates of distributions rather than point estimates to overcome this limitation,[215, 230] but the research is scarce and it is unclear whether the results obtained by using this approach are accurate representations of reality.

A second limitation results from inequivalence between the reference sets and the health states in the consequences table. In many cases, the description of a health state in the reference set was different to that in the consequences table, as is evident in Table 43. The strong correlation between the reference utilities and those derived from the EQ-5D suggests that this limitation is unlikely to be a significant issue. However, not every consequence was included in this analysis and so there may be outliers that were not identified.

Related to this is a further limitation that some of the health states described in the consequences table are generalisations for heterogeneous conditions which may have substantially variable effects on QOL. It has been found that differences in descriptions or specificity of health states may result in differences in the utilities measured.[232] For example, QOL in patients experiencing the consequence of "stroke" may be dependent upon the presence or absence of any impairment/s, the degree of impairment, whether the impairment is permanent or temporary, and whether there was motor,

language or cognitive deficits. The use of PSA may alleviate this issue to some extent, although it is likely that this would not entirely overcome this issue. Consequently, the utilities must only be considered broad approximations of the QOL of patients experiencing the health state.

4.5 Conclusion

The general aim of the research described in Chapters 3 and 4 of this thesis was to improve the validity and applicability of the consequences table initially formulated by Tenni. Two studies were undertaken to achieve this aim, and the results of these studies suggest that the aim was achieved. The outcome of this research was an updated table of common clinical consequences with estimates of QOL lost and health resource costs incurred should a patient experience one or more of these consequences.

Whilst the estimates of these parameters appeared plausible and reasonable, any economic evaluation which is undertaken using this data should be aware of and take into consideration the limitations of this approach. Despite these limitations, the findings of this research should be of substantial value in future economic evaluations in this area, and represent a significant step forward in improving the quality of economic evaluations in this area, where empirical evidence concerning the counterfactual state is not available.

Having undertaken this research, it was possible to proceed with the planned evaluation of HMRs to investigate their clinical and economic outcomes. The results of this evaluation are presented in the proceeding chapters.

A CLINICAL AND ECONOMIC EVALUATION OF MEDICATION REVIEWS CONDUCTED BY PHARMACISTS FOR COMMUNITY-DWELLING AUSTRALIANS

Volume Two

Andrew Stafford BPharm(Hons) MPS AACPA

Chapter 5 - Results of the VALMER study: characteristics of pharmacists, patients and drug-related problems

5.1 Overview

This is the first of two chapters in which the results of the VALMER study are presented. This chapter describes the characteristics of the accredited pharmacists who participated in the study, the characteristics of the patients for whom they undertook HMRs, and the DRPs identified by the pharmacists. Chapter 6 presents the results of the clinical and economic evaluation of the HMRs.

Data collection for the VALMER study commenced on 27 March 2008, and concluded on 14 November 2008. During this time, 203 pharmacists completed an enrolment form, indicating that they would be prepared to submit HMRs for the study. At the conclusion of the data collection period, 149 pharmacists had contributed 675 HMRs. Nine HMRs were excluded from the sample as they were conducted prior to the project start date, as per the exclusion criteria (Section 2.1.3.2). Another five HMRs contained no data regarding the patient's medications or medical history and were also excluded, resulting in a final sample of 661 HMRs. Of these 661 HMRs, outcomes data were included with 560 (84.7%). With regard to the survey of participating pharmacists, 117 of the 149 pharmacists (78.5%) who submitted HMRs for the study completed the survey.

This is shown in Figure 36.

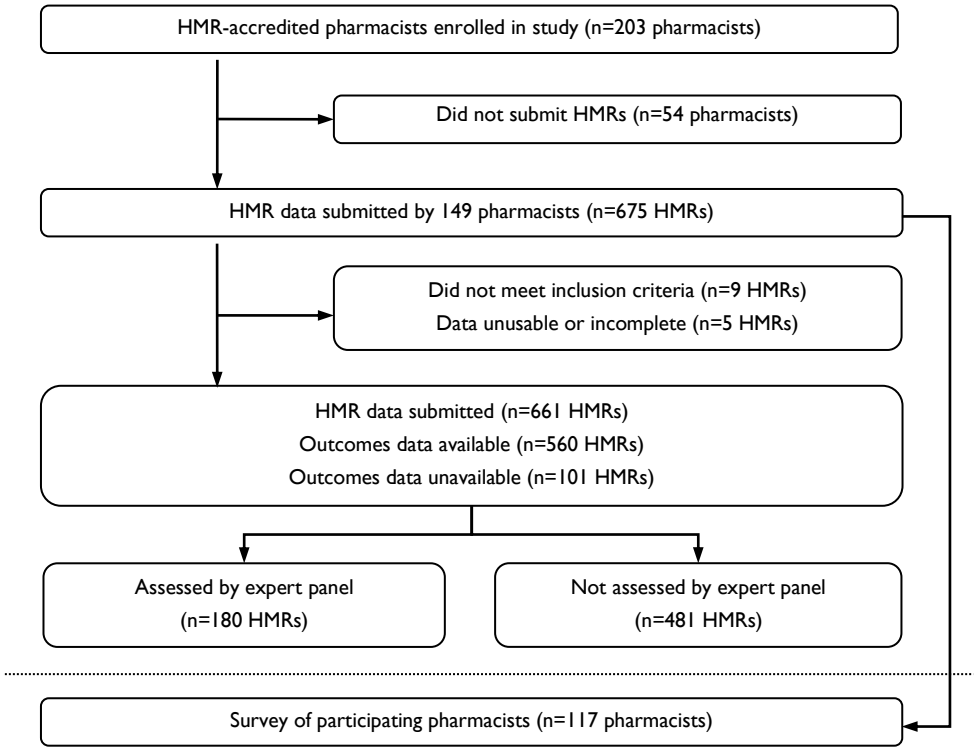

FIGURE 36 - VALMER STUDY FLOW CHART

The number of HMRs submitted by the pharmacists is shown in Table 49. Over 80% of the HMRs were provided by pharmacists who submitted the maximum of five HMRs.

TABLE 49 - NUMBER OF HMRS SUBMITTED BY PHARMACISTS

NUMBER OF HMRS SUBMITTED	NUMBER (%) OF PHARMACISTS
1	5 (3.4%)
2	10 (6.7%)
3	11 (7.4%)
4	12 (8.1%)
5	111 (74.5%)
TOTAL	**149 (100.0%)**

5.2 Participating pharmacists

5.2.1 General pharmacist demographics

Every pharmacist who participated in the VALMER study was accredited to perform medication reviews with AACP; no SHPA-accredited pharmacist submitted HMRs for the study. The main state of practice of the pharmacists who participated in the study is shown in Figure 37. Each Australian state or territory was represented by at least one pharmacist. A χ^2 goodness-of-fit test indicated that the proportion of pharmacists in the study group according to their main state of practice was not consistent with the entire population of AACP-accredited pharmacists (χ^2=120.95, df=7, P<0.001). When compared to the national number of AACP-accredited pharmacists, a greater proportion of Victorian and Tasmanian pharmacists participated in the study, potentially due to local awareness of the study.

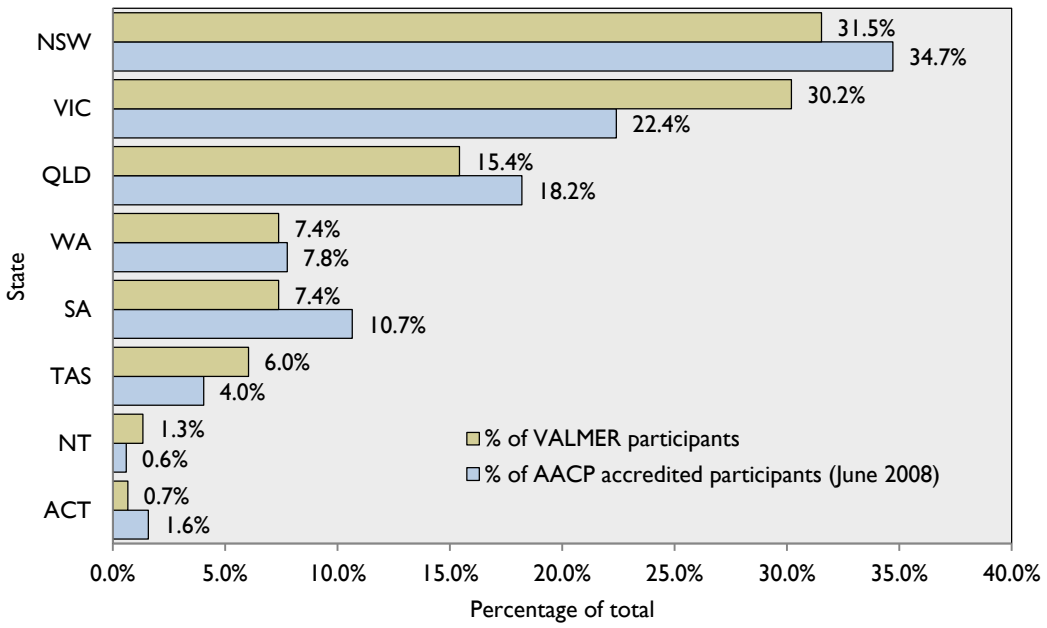

FIGURE 37 - PERCENTAGE OF PHARMACISTS PARTICIPATING IN VALMER ACCORDING TO THEIR MAIN STATE OF PRACTICE

Of the 149 pharmacists who submitted HMRs, 117 (78.5%) completed the survey. Non-respondents were either not contactable due to them being out of the country or declined to participate. The general characteristics of the survey respondents are

presented in Table 50. Male pharmacists accounted for less than a quarter of participants. The majority of both males and females (91%) were from community pharmacy backgrounds, such as proprietors or employees.

TABLE 50 - CHARACTERISTICS OF PHARMACISTS WHO PARTICIPATED IN THE VALMER STUDY

CHARACTERISTIC	MALE (N=27, 23.1%)	FEMALE (N=90, 76.9%)	TOTAL (N=117)
Year of completion of initial pharmacist training			
• Median (IQR)	1983.5 (27)	1989 (20)	1988 (21)
• Range	1963-2006	1967-2007	1963-2007
Year of initial AACP accreditation			
• Median (IQR)	2003 (4)	2003 (5)	2003 (5)
• Range	1997-2008	1996-2008	1996-2008
Area of main employment (number, % of total)			
• Community pharmacy proprietor	4 (14.8%)	7 (7.8%)	11 (9.4%)
• Community pharmacy employee	5 (18.5%)	28 (31.1%)	33 (28.2%)
• Provider of medication reviews	10 (37.0%)	28 (31.1%)	38 (32.5%)
• Hospital pharmacy employee	2 (7.4%)	7 (7.8%)	9 (7.7%)
• Other (e.g. NPS facilitators, academia)	6 (22.2%)	20 (22.2%)	26 (22.2%)
Median number of HMRs completed [range]			
• Ever	300 [12 - 1090]	217 [4-2500]	235 [4 - 3500]
• In 2008	73 [4 - 1090]	59 [2 - 500]	60 [2 - 1090]

The country and Australian states where the pharmacists completed their pharmacy-related undergraduate education is summarised in Table 51. Somewhat predictably, over 80% of the survey respondents had completed their undergraduate training in Australia.

TABLE 51 - UNDERGRADUATE EDUCATION HISTORY OF PHARMACISTS WHO PARTICIPATED IN THE VALMER STUDY

COUNTRY OF UNDERGRADUATE DEGREE	NUMBER (% OF TOTAL)		
	MALE	FEMALE	TOTAL
Australia	**22 (18.8)**	**76 (65.0)**	**98 (83.8)**
• New South Wales	8 (6.8)	26 (22.2)	34 (29.1)
• Queensland	2 (1.7)	14 (12.0)	16 (13.7)
• South Australia	4 (3.4)	2 (1.7)	6 (5.1)
• Tasmania	2 (1.7)	6 (5.1)	8 (6.8)
• Victoria	5 (4.3)	20 (17.1)	25 (21.4)
• Western Australia	1 (0.9)	8 (6.8)	9 (7.7)
Overseas	**2 (1.7)**	**13 (11.1)**	**15 (12.8)**
• New Zealand	(0.0)	5 (5.6)	5 (4.3)
• Pakistan	(0.0)	1 (1.1)	1 (0.9)
• Russia	(0.0)	1 (1.1)	1 (0.9)
• South Africa	(0.0)	1 (1.1)	1 (0.9)
• United Kingdom	2 (7.4)	4 (4.4)	6 (5.1)
• United States of America	(0.0)	1 (1.1)	1 (0.9)
(No response)	**3 (2.6)**	**1 (0.9)**	**4 (3.4)**
TOTAL	**27 (23.1)**	**90 (76.9)**	**117 (100)**

Approximately one quarter of the pharmacists had completed some form of postgraduate training (in addition to AACP accreditation), the majority of which were postgraduate diplomas (Table 52).

TABLE 52 - POSTGRADUATE QUALIFICATIONS OF PHARMACISTS WHO PARTICIPATED IN THE VALMER STUDY

HIGHEST LEVEL OF POSTGRADUATE QUALIFICATION	NUMBER (% OF TOTAL)		
	MALE	FEMALE	TOTAL
None	20 (74.1)	61 (67.8)	81 (69.2)
Postgraduate diploma	3 (11.1)	19 (21.1)	22 (18.8)
Masters	4 (14.8)	4 (4.4)	8 (6.8)
Doctor of philosophy	0 (0.0)	2 (2.2)	2 (1.7)
Other (e.g. clinical certificate)	0 (0.0)	4 (4.4)	4 (3.4)
TOTAL	**27 (23.1)**	**90 (76.9)**	**117 (100)**

5.2.2 Clinical performance

5.2.2.1 Accreditation and reaccreditation examinations

5.2.2.1.1 Accredited pharmacists Australia-wide

Multiple choice scores for their initial attempt at accreditation or reaccreditation with AACP were available for 1213 pharmacists. These examinations took place between March 2007 and June 2009. Descriptive statistics for these results are presented in Table 53. Over 90% of the pharmacists passed the assessment on their first attempt, with the mean score being 42.3 out of a possible 50. A consideration with these results is that not all pharmacists who undertook these examinations re-sat the exam to achieve accreditation. Consequently, the mean score for accredited pharmacists (that is, those who completed accreditation) may be slightly higher than these figures indicate.

5.2.2.1.2 Study participants

During the period of data collection, 97 of the 149 pharmacists who participated in the study (65.1%) undertook the accreditation and reaccreditation examinations. Descriptive statistics and comparisons between the VALMER study pharmacists and the entire sample are presented in Table 53. No pharmacist who participated in the VALMER study failed to achieve a passing score in their first attempt. Consequently, the mean examination score for the study pharmacists was significantly higher than that of non-participants, although the absolute difference was very small.

TABLE 53 - SCORES FOR AACP ACCREDITATION AND REACCREDITATION EXAMINATIONS FOR VALMER PHARMACISTS COMPARED TO NON-PARTICIPANTS

PARAMETER	VALMER PARTICIPANTS (N=97)	NON-PARTICIPANTS (N=1116)	TEST RESULTS
Mean score (/50) ± SD [range]	43.1 ± 3.2 [37 - 50]	42.2 ± 3.9 [31 - 50]	t=2.15, df=1211, P=0.03*
Median score (/50) [interquartile range]	43 [4]	43 [5]	-
Number (%) passed on first attempt	97 (100)	1008 (90.3)	χ^2=8.06, df=1, P=0.001**

*Independent samples t-test; **Pearson χ^2 test

Despite the statistical differences in mean score and proportion passing on their first attempt, it is unlikely to be of importance given the small magnitude (0.9 of one mark out of 50). Consequently, it was concluded from this analysis that the clinical knowledge of the VALMER pharmacists, at least as measured by their accreditation and reaccreditation examination scores, was aligned with the greater body of AACP-accredited pharmacists.

5.2.2.2 Continuing education activity

Substantial efforts were made to recruit pharmacists to participate in the VALMER study at the three largest accredited pharmacist continuing-education events in 2008. These events were as follows:

- the accredited pharmacist forum at the Australian Professional Pharmacy Conference, Gold Coast, Queensland (27 March 2008),
- AACP Consultant Pharmacy Clinical Seminar, Adelaide (29 May - 1 June 2008), and
- the accredited pharmacist forum at the Pharmacy Australia Congress, Perth (24 October 2008).

It was considered that the pharmacists who attended these events may not have been representative of the greater body of accredited pharmacists - their attendance may have indicated greater activity in continuing education activities and perhaps resulted in them producing HMRs of a generally higher quality. To address whether this may have potentially confounded the results of the VALMER study, the survey investigated their attendances at these events.

One hundred and thirteen pharmacists responded to this question, and the results are presented in Figure 38. Two thirds of participants did not attend any of these continuing education events, and less than 9% of the participating pharmacists attended two or more of these events in 2008.

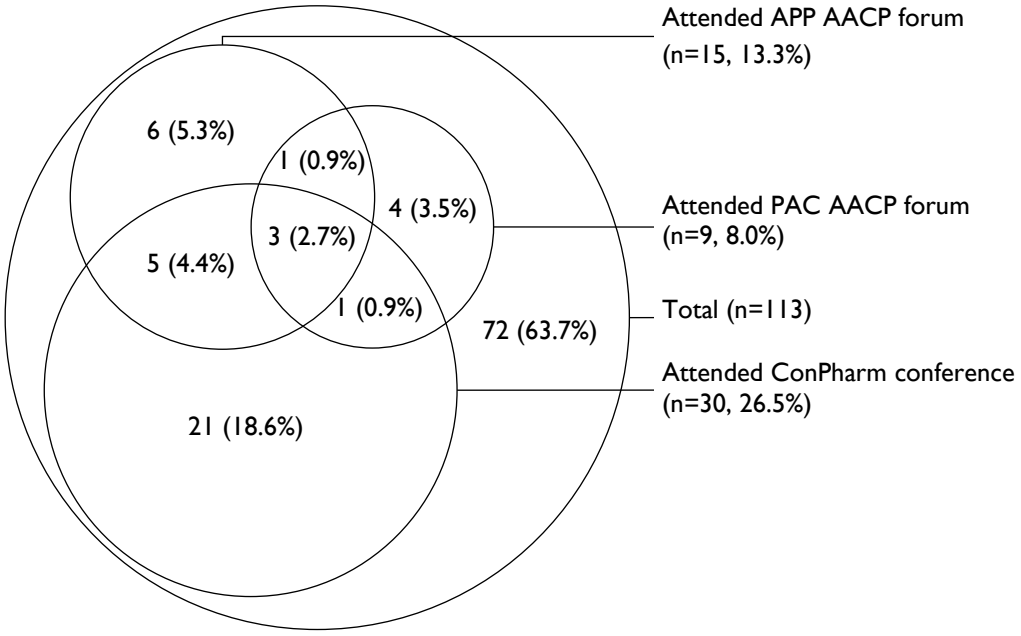

FIGURE 38 - ATTENDANCE OF VALMER PARTICIPANTS AT CONTINUING EDUCATION EVENTS DURING 2008

In consideration of these data, it was concluded that advertising for the study at these continuing education events was unlikely to have markedly affected the recruitment of pharmacists with different characteristics to the greater body of accredited pharmacists.

The pharmacists were asked to estimate the number of hours of pharmacy-related continuing education activities they undertook on an annual basis. The results of this question are shown in Table 54.

TABLE 54 - HOURS OF CONTINUING EDUCATION UNDERTAKEN ANNUALLY BY PARTICIPATING PHARMACISTS

PARAMETER	HOURS
Mean ± SD [range]	86 ± 75 [2 - 400]
Median [interquartile range]	60 [60]

The pharmacists who attended at least one of the three continuing education events discussed above undertook more continuing education than those who did not attend any of the conferences (median 80 hours compared to 50 hours; Mann Whitney U=1075.5, Z=-2.404, P=0.016). Nonetheless, the majority of the pharmacists who participated in the study undertook a substantial amount of continuing education activities.

5.2.3 Interaction with General Practitioners

To characterise the pharmacists' experiences with GPs, the pharmacists were asked to estimate the frequency with which they discussed HMRs with the referring GP, and their perceived value of this communication. Their responses to this section of the survey are shown in Table 55. Whilst over three quarters of the surveyed pharmacists indicated that they moderately or extremely valued communication with the GP, a similar proportion of the pharmacists (76%) indicated that this occurred for less than half of the HMRs they performed.

TABLE 55 - FREQUENCY AND VALUE OF COMMUNICATION WITH GENERAL PRACTITIONERS REPORTED BY PHARMACISTS

FREQUENCY OF COMMUNICATION	VALUE OF COMMUNICATION - NUMBER (% OF TOTAL) RESPONDENTS					
	EXTREME	MODERATE	SOME	MINIMAL	UNSURE	TOTAL
Never	4 (3.4)	7 (6.0)	4 (3.4)	2 (1.7)	0	**17 (14.5)**
Around a quarter of the time	36 (30.8)	25 (21.4)	10 (8.5)	1 (0.9)	0	**72 (61.5)**
About half the time	5 (4.3)	5 (4.3)	2 (1.7)	0	0	**12 (10.3)**
Around three quarters of the time	6 (5.1)	0	0	0	0	**6 (5.1)**
Always	3 (2.6)	0	0	0	0	**3 (2.6)**
Unsure	0	0	0	0	7 (6.0)	**7 (6.0)**
Total	**54 (46.2)**	**37 (31.6)**	**16 (13.7)**	**3 (2.6)**	**7 (6.0)**	**117 (100)**

5.2.4 Focus on particular HMR-related tasks

The survey contained a series of questions that investigated the pharmacists' approach towards undertaking HMRs. These questions broadly encompassed the various tasks associated with HMRs as described in the Pharmaceutical Society of Australia's guidelines for pharmacists providing HMR services (discussed in Section 1.2.2.1).

A summary of the responses of the 110 pharmacists who completed this part of the survey is shown in Table 56. For the majority of the processes, the most frequent response was that the greatest emphasis was placed upon it. In particular, more respondents focussed on assessing the clinical appropriateness of therapy than any other task. Interestingly, whilst most respondents placed a similarly high level of emphasis on the identification of ADRs, several respondents placed only *Minimal* or *Some* emphasis on this task.

TABLE 56 - PHARMACISTS' SELF-REPORTED APPROACH TOWARDS UNDERTAKING VARIOUS TASKS ASSOCIATED WITH HMRS

HMR PROCESS	USUAL EMPHASIS PLACED ON PROCESS (NUMBER (%) OF RESPONDENTS, N=110)				
	NONE	MINIMAL	SOME	MODERATE	MOST
Checking compliance	0 (0.0)	0 (0.0)	8 (7.3)	45 (40.9)	**57 (51.8)**
Providing patient education (e.g. counselling, confusion regarding generics, pricing etc.)	0 (0.0)	0 (0.0)	1 (0.9)	38 (34.5)	**71 (64.5)**
Assessing clinical appropriateness of drug therapy (e.g. doses rational, therapy consistent with current guidelines, identifying untreated indications)	0 (0.0)	0 (0.0)	5 (4.5)	22 (20.0)	**83 (75.5)**
Removing out of date and unnecessary prescriptions and repeat forms	5 (4.5)	12 (10.9)	33 (30.0)	**39 (35.5)**	21 (19.1)
Identifying adverse drug reactions	0 (0.0)	2 (1.8)	5 (4.5)	30 (27.3)	**73 (66.4)**
Checking administration equipment and technique (e.g. nebulisers, inhalers)	0 (0.0)	2 (1.8)	10 (9.1)	**58 (52.7)**	40 (36.4)
Ensuring adequate therapeutic monitoring	0 (0.0)	3 (2.7)	20 (18.2)	**48 (43.6)**	39 (35.5)

Each row totals 110 responses (100%)

The pharmacists were also asked to what extent they prioritised the DRPs they identify in HMRs. This was to test the assumption made in the study that most

pharmacists prioritise the DRPs identified in HMRs from most to least clinically relevant. The majority responded that they *Always* (78, 70.9%) or *Usually* (25, 22.7%) prioritise the DRPs they identify, and few pharmacists prioritised the DRPs *About half the time* (2, 1.8%) or *Sometimes* (5, 4.5%). Based on this data, it seemed probable that the majority of pharmacists had prioritised the DRPs that they identified in the HMRs they submitted for the VALMER study. As the economic evaluation of the HMRs involved the experts assessing only the first three DRPs identified in each HMR, the results of this part of the survey suggest that the most clinically relevant DRPs (in the opinion of the pharmacist who performed the HMR) were those assessed by the experts for most of the HMRs. Consequently, it is reasonable to assume that the majority of the benefits resulting from each HMR would have resulted from addressing these DRPs, so the expert assessment was likely to capture most of the benefit resulting from the HMRs.

5.2.5 Use of medication-review software

The participating pharmacists were asked to indicate whether or not they used any medication-review specific computer software to assist them with HMRs. Of the 109 pharmacists who answered this question, 23 (21%) indicated that they used a software system. Aside from a solitary pharmacist who used MedsIndex (a non-medication review-specific compliance measurement tool incorporated in dispensing systems), each pharmacist who used software utilised MediFlags (Australian Medicines Handbook Pty Ltd, Adelaide, South Australia).

The tasks for which the pharmacists used medication review software and the frequency with which they used it are shown in Table 57.

TABLE 57 - FREQUENCIES WITH WHICH PHARMACISTS USED MEDICATION REVIEW SOFTWARE SYSTEMS TO PERFORM DIFFERENT TASKS.

TASK	FREQUENCY OF USE (NUMBER (%) OF RESPONDENTS, N=23)				
	ALWAYS	FREQUENTLY	ABOUT HALF THE TIME	SOMETIMES	NEVER
Record keeping	**17 (73.9)**	2 (8.7)	2 (8.7)	1 (4.3)	1 (4.3)
Formatting report	**21 (91.3)**	0 (0.0)	1 (4.3)	0 (0.0)	1 (4.3)
Improving knowledge	5 (21.7)	1 (4.3)	1 (4.3)	**9 (39.1)**	7 (30.4)
Identifying DRPs	5 (21.7)	2 (8.7)	4 (17.4)	**9 (39.1)**	3 (13.0)

Each row totals 23 responses (100%)

It is apparent that the majority of respondents used the software mainly for record keeping and formatting of reports, with fewer pharmacists relying on it for identification of DRPs.

5.2.6 Effect of the DVA Dosage Administration Aid Program

In early 2008, the DVA commenced a program of subsidising dosage administration aids (DAAs) for eligible veterans.[253] The initial implementation of this program required every veteran who was to receive the service to have a HMR prior to its commencement[xvii]. Data collection for the VALMER study commenced shortly after the DAA program was introduced, hence many of the HMRs included in the study may have been performed for this indication alone. This introduced a potential confounder for study for the following reasons:

- Patients may have received a HMR prior to the commencement of the DAA program, and were referred for another HMR shortly afterwards simply to commence a DAA. This may have limited the potential benefits of the second HMR (which was submitted for the VALMER study), resulting in an underestimation of the benefits of a "typical" HMR;

[xvii] This restriction has now been changed - a HMR is no longer a requirement for the DAA service, although DVA continue to strongly recommend that veterans be assessed via HMR as part of the DAA program

- Given that the patient was considered eligible of a DAA, they may have been at a greater risk of medication misadventure than a "typical" HMR patient. This could potentially result in an overestimation of the benefits of HMRs; and
- GPs who would not normally refer patients for HMRs may have had to do so to arrange DAAs. The effect of this may have been variable, in that the GP may be more or less receptive to any recommendations resulting from the HMR, resulting in an unpredictable effect on the results of the VALMER study.

To assess the possible influence of the DAA program on the HMRs submitted for the VALMER study, the survey asked pharmacists about the HMRs that they performed as part of the DVA DAA program. Eighty five pharmacists (72.6% of respondents) had performed at least one DAA HMR. The results of their responses to these questions are presented in Table 58.

TABLE 58 - PHARMACIST VIEWS OF DIFFERENCES BETWEEN DVA DAA HMRS AND "NORMAL" HMRS

PARAMETER	DIFFERENCE TO A "NORMAL" HMR (NUMBER (%) OF TOTAL RESPONDENTS)				
	SUBSTANTIALLY MORE	SOMEWHAT MORE	ABOUT THE SAME	SOMEWHAT LESS	SUBSTANTIALLY LESS
Complexity	2 (2.4)	9 (10.6)	**67 (78.8)**	6 (7.1)	1 (1.2)
Number of clinical issues	1 (1.2)	10 (11.8)	**67 (78.8)**	6 (7.1)	1 (1.2)
Number of compliance issues	3 (3.5)	17 (20.0)	**55 (64.7)**	8 (9.4)	2 (2.4)
Potential to improve health	10 (11.8)	22 (25.9)	**52 (61.2)**	1 (1.2)	0

Each row totals 85 responses (100%)

It was apparent that the majority of the pharmacists believed that there were few differences between the HMRs that they had performed as part of the DVA DAA program and "normal" HMRs in any of the parameters assessed. The greatest potential for confounding appeared to be in relation to compliance issues and a perceived overall potential to improve health, where a greater proportion of pharmacists believed that the DVA DAA HMRs were more likely to improve health and compliance than other HMRs that they perform.

5.2.7 Time to perform HMRs

Information regarding the time taken to perform the HMRs submitted for the study was provided by 138 pharmacists (92.6%) for 600 of the HMRs (90.8%). The patient interview was not performed by the accredited pharmacist in two HMRs, and consequently time data was not provided for these HMRs. Descriptive statistics of the various tasks involved in performing the HMRs are shown in Table 59.

TABLE 59 - TIME FOR HMR-ASSOCIATED TASKS

HMR-ASSOCIATED TASK	TIME (MINUTES)	
	MEDIAN (IQR)	RANGE
Pre-interview preparation		
• All respondents (n=600)	20 (20)	0 - 120
• Reported other than 0 (n=573)	20 (15)	1 - 120
Interview	60 (15)	15 - 180*
Travel		
• All respondents (n=600)	20 (30)	0 - 420
• Reported other than 0 (n=570)	20 (25)	2 - 420
Assessment Report	60 (45)	10 - 300
Total "other" time		
• All respondents (n=600)	0 (0)	0 - 100
• Reported other than 0 (n=137)	15 (20)	5 - 100
Total HMR time	**175 (95)**	**40 - 535**

* Interview not performed by the reviewing pharmacist in two HMRs

Aside from travel, the task with the greatest variation between pharmacists involved writing the clinical assessment report. Activities documented by pharmacists in the "Other" category included a variety of tasks, including:

- Liaising with health professionals and carers for more information about the patient;
- Discussing the HMR with the referring GP;
- Researching aspects specific to the HMR;
- Administrative paperwork; and

- Demonstration of medicinal devices such as glucometers and point of care monitors for warfarin therapy.

5.3 Patient characteristics

The general characteristics of the patients who received HMRs in the VALMER study are summarised in Table 60. Female patients constituted a majority (58%) of the study population. There was a broad range of patient ages, although patients aged 65 years or older accounted for over 85% of the patient group. Seventeen HMR referrals did not contain any information regarding the patient's medical conditions; over half of the patients (53.1%) had between five and ten diagnosed medical conditions.

The lowest number of medications taken was two; 60.1% of the patients were using between eight and fourteen medications. Excluding medications taken on a when-required basis, all but 39 patients (5.9%) were taking five or more regular medications, and 75% of the patients were using between five and twelve preparations on a regular basis.

TABLE 60 - GENERAL PATIENT DEMOGRAPHICS

CHARACTERISTIC	MALE N=278 (42.1%)	FEMALE* N=383 (57.9%)	TOTAL N=661
Age			
Median (IQR) [range] - years	77 (13) [30 - 96]	79 (12) [30 - 98]	78 (13) [30 - 98]
• Number (% of total) aged <65 years	47 (7.1)	46 (7.0)	93 (14.1)
• Number (% of total) aged 65 to 75 years	74 (11.2)	81 (12.3)	155 (23.4)
• Number (% of total) aged >75 years	157 (23.8)	254 (38.4)	411 (62.2)
Documented medical conditions**	8.4 ± 4.9 [0 - 33]	9.1 ± 5.2 [0 - 29]	8.9 ± 5.1 [0 - 33]
Number of medications			
• Total (incl. when required and complementary preparations) **	11.1 ± 4.4 [2 - 28]	12.2 ± 4.5 [4 -30]	11.8 ± 4.5 [2 - 28]
• Taken on a regular basis**	9.1 ± 3.7 [1 - 22]	9.9 ± 3.9 [2 - 22]	9.6 ± 3.8 [1 - 22]

*Age not provided for two female patients; ** mean ± SD [range]

Table 61 compares the general demographics of the patients who received HMRs in the VALMER study to those of the patients reviewed in four of the five QUM Evaluation

Program projects conducted in the 1990s (there was insufficient documentation in the study by Greenhill[136]). The characteristics of the patients in two of the larger, more recent studies of HMRs are also presented for comparison.

TABLE 61 - COMPARISON OF GENERAL PATIENT DEMOGRAPHICS BETWEEN THE VALMER STUDY AND PREVIOUS HMR-RELATED PROJECTS

STUDY	CHARACTERISTIC (MEAN ± SD [RANGE] UNLESS STATED OTHERWISE)			
	MALE PATIENTS (%)	AGE (YEARS)	MEDICAL CONDITIONS	DRUGS
VALMER study (n=661)	42.1	76.0 ± 10.4 [30 - 98]	8.9 ± 5.1 [0 - 33]	11.8 ± 4.5 [2 - 28]
Domiciliary Medication Review Project[66] (n=176)†	37.9	72.3 [37 - 100]	not reported	9.1
Sutherland Project[140] (n=170)††	43	71 ± 16	5.0 ± 1.9	8.5 ± 3.0
QUMCIT[86] (n=500)†††	39.6	74*	5.7	9.0 [2 - 21]
St. George Canterbury Medico/Pharmacy Project[142] (n=362)	40	71.9 [25 - 95	5.4	10.7 [2 - 21]
Stafford *et al*. 2009[68] (n=138)	44.2	73.9 ± 10.6	7.8 ± 4.4 [1 - 27]	11.7 ± 4.2 [4 - 25]
Castelino *et al*. 2010[254] (n=270)	44.8	75.3 ± 7.4	6.7 ± 2.8	11.6 ± 4.1

*Median; †Patients who received HMRs; ††Patients in Stage 2 only (less documentation of Stage 1 patient characteristics); †††Detail provided for only 500 of the 1000 patients who received HMRs

From the data presented in Table 61, it is apparent that the demographics of the patients reviewed in the VALMER study were generally consistent with those reported in previous studies. However, it is notable that the VALMER study patients were documented with slightly more medical conditions than those in the previous studies. This may have resulted from variations in the source of these data, which included patient-reported conditions, medical notes and HMR reports. It is also noteworthy that the number of drugs taken by the VALMER study patients was greater than in the QUM Evaluation Program projects, but consistent with the more recent studies, most likely due to changes in prescribing guidelines and a greater number of drugs becoming available in recent years. As the characteristics of the patients who received

HMRs in the VALMER study were generally consistent with those in previous studies of HMRs, it seems reasonable to assume that the patients in the VALMER study were likely to be representative of patients who receive HMRs in usual practice.

5.3.1 Diagnosed conditions

The HMR referrals documented a total of 5846 medical conditions. Table 62 lists the most common diagnosed medical conditions in the patient group, grouped by their ICPC2-PLUS chapter. The most common diagnoses were cardiovascular conditions, such as hypertension, ischaemic heart disease and atrial fibrillation. Correspondingly, the prevalence of metabolic diseases that are significant risk factors for these illnesses, such as diabetes mellitus and hyperlipidaemia, was also high. Musculoskeletal diseases were also common diagnoses, of which osteoarthritis and osteoporosis were the most prevalent conditions.

TABLE 62 - PREVALENCE OF PATIENTS' MEDICAL CONDITIONS - ICPC2-PLUS
CHAPTER GROUPS AND MOST COMMON INDIVIDUAL CONDITIONS

GROUP OF CONDITION (ICPC2 CHAPTER GROUPING) / MOST FREQUENT INDIVIDUAL CONDITIONS	NUMBER OF PATIENTS (% OF TOTAL)		
	MALES N=278 (42.1)	FEMALES N=383 (57.9)	TOTAL N=661
Cardiovascular	**235 (35.6)**	**312 (47.2)**	**547 (82.8)**
Hypertension, uncomplicated	154 (23.3)	248 (37.5)	402 (60.8)
Ischaemic heart disease without angina	77 (11.6)	60 (9.1)	137 (20.7)
Atrial fibrillation/flutter	62 (9.4)	58 (8.8)	120 (18.2)
Heart failure	43 (6.5)	49 (7.4)	92 (13.9)
Stroke/cerebrovascular accident	26 (3.9)	43 (6.5)	69 (10.4)
Endocrine, metabolic and nutritional	**200 (30.3)**	**257 (38.9)**	**457 (69.1)**
Lipid disorder	102 (15.4)	168 (25.4)	270 (40.8)
Diabetes, non-insulin dependent	102 (15.4)	113 (17.1)	215 (32.5)
Gout	49 (7.4)	25 (3.8)	74 (11.2)
Vitamin/nutritional deficiency	21 (3.2)	34 (5.1)	55 (8.3)
Hypothyroidism/myxoedema	9 (1.4)	39 (5.9)	48 (7.3)
Musculoskeletal	**150 (22.7)**	**271 (41.0)**	**421 (63.7)**
Osteoarthrosis, other	61 (9.2)	122 (18.5)	183 (27.7)
Osteoporosis	33 (5.0)	112 (16.9)	145 (21.9)
Fracture: other	16 (2.4)	40 (6.1)	56 (8.5)
Back syndrome without radiating pain	22 (3.3)	31 (4.7)	53 (8.0)
Back syndrome with radiating pain	14 (2.1)	30 (4.5)	44 (6.7)
Digestive	**145 (21.9)**	**206 (31.2)**	**351 (53.1)**
Oesophagus disease	78 (11.8)	117 (17.7)	195 (29.5)
Diverticular disease	15 (2.3)	45 (6.8)	60 (9.1)
Hiatus hernia	9 (1.4)	20 (3.0)	29 (4.4)
Peptic ulcer, other	14 (2.1)	14 (2.1)	28 (4.2)
Benign/uncertain neoplasm digestive	12 (1.8)	15 (2.3)	27 (4.1)
Psychological	**122 (18.5)**	**143 (21.6)**	**265 (40.1)**
Depressive disorder	48 (7.3)	71 (10.7)	119 (18.0)
Tobacco abuse	41 (6.2)	37 (5.6)	78 (11.8)
Sleep disturbance	27 (4.1)	39 (5.9)	66 (10.0)
Dementia (incl senile, Alzheimer's)	13 (2.0)	8 (1.2)	21 (3.2)
Chronic alcohol abuse	12 (1.8)	4 (0.6)	16 (2.4)
General & unspecified	**80 (12.1)**	**157 (23.8)**	**237 (35.9)**
Allergy/allergic reaction NOS	54 (8.2)	130 (19.7)	184 (27.8)
Effect of prosthetic device	18 (2.7)	13 (2.0)	31 (4.7)
Abnormal result investigation NOS	8 (1.2)	12 (1.8)	20 (3.0)
Respiratory	**99 (15.0)**	**117 (17.7)**	**216 (32.7)**
Chronic obstructive pulmonary disease	60 (9.1)	44 (6.7)	104 (15.7)
Asthma	32 (4.8)	67 (10.1)	99 (15.0)
Respiratory disease, other	10 (1.5)	11 (1.7)	21 (3.2)
Allergic rhinitis	9 (1.4)	11 (1.7)	20 (3.0)
Eye	**56 (8.5)**	**103 (15.6)**	**159 (24.1)**
Glaucoma	15 (2.3)	30 (4.5)	45 (6.8)
Eye/adnexa disease, other	11 (1.7)	29 (4.4)	40 (6.1)
Macular degeneration	8 (1.2)	23 (3.5)	31 (4.7)
Cataract	12 (1.8)	18 (2.7)	30 (4.5)
Urological	**53 (8.0)**	**101 (15.3)**	**154 (23.3)**
Urinary disease, other	27 (4.1)	55 (8.3)	82 (12.4)
Cystitis/urinary infection, other	3 (0.5)	17 (2.6)	20 (3.0)
Incontinence urine	5 (0.8)	15 (2.3)	20 (3.0)
Skin	**48 (7.3)**	**86 (13.0)**	**134 (20.3)**

GROUP OF CONDITION (ICPC2 CHAPTER GROUPING) MOST FREQUENT INDIVIDUAL CONDITIONS	NUMBER OF PATIENTS (% OF TOTAL) MALES N=278 (42.1)	 FEMALES N=383 (57.9)	 TOTAL N=661
Malignant neoplasm of skin	21 (3.2)	27 (4.1)	48 (7.3)
Dermatitis, contact/allergic	10 (1.5)	21 (3.2)	31 (4.7)
Neurological	**44 (6.7)**	**77 (11.6)**	**121 (18.3)**
Vertigo/dizziness	9 (1.4)	13 (2.0)	22 (3.3)
Peripheral neuritis/neuropathy	10 (1.5)	8 (1.2)	18 (2.7)
Male genital	**54 (8.2)**	**18 (2.7)**	**72 (10.9)**
Malignant neoplasm prostate	25 (3.8)	0 (0.0)	25 (3.8)
Ear	**25 (3.8)**	**34 (5.1)**	**59 (8.9)**
Vertiginous syndrome	6 (0.9)	11 (1.7)	17 (2.6)
Blood, blood forming organs & immune mechanism	**19 (2.9)**	**35 (5.3)**	**54 (8.2)**
Iron deficiency anaemia	5 (0.8)	16 (2.4)	21 (3.2)
Anaemia, other/unspecified	5 (0.8)	11 (1.7)	16 (2.4)
Female genital	**0 (0.0)**	**32 (4.8)**	**32 (4.8)**
Menopausal symptom/complaint	0 (0.0)	14 (2.1)	14 (2.1)

NOS - Not otherwise specified

5.3.2 Medications taken

The patients were documented as taking a total of 7790 medications, including when-required and complementary preparations. The medications most commonly taken are shown in Table 63. Given the high prevalence of cardiovascular disease amongst the patients, the high proportion of patients taking medications which manage these conditions is unsurprising. Three quarters of the patients were taking a lipid modifying agent, of which atorvastatin was the most common.

The prevalence of musculoskeletal disease in the patients was also high. Correspondingly, many patients were taking analgesics, the most common of which was paracetamol. The proportion of patients taking non-steroidal anti-inflammatory agents was substantially lower than those taking paracetamol, and the two most commonly used NSAIDs were COX-II specific agents. Notably, almost 60% of the patients were taking a medication to treat a disorder related to gastric-acid, such as proton-pump inhibitors.

TABLE 63 - INDIVIDUAL MEDICATIONS TAKEN MOST FREQUENTLY AND PREVALENCE OF EACH ATC LEVEL 2 GROUP OF MEDICATION

ATC LEVEL 2 MEDICATION GROUP	NUMBER OF PATIENTS TAKING (% OF TOTAL)		
MOST FREQUENT INDIVIDUAL MEDICATIONS (ATC LEVEL 5)	MALES N=278 (42.1)	FEMALES N=383 (57.9)	TOTAL N=661
Lipid modifying agents	**205 (31.0)**	**275 (41.6)**	**480 (72.6)**
Atorvastatin	90 (13.6)	116 (17.5)	206 (31.2)
Simvastatin	56 (8.5)	65 (9.8)	121 (18.3)
Omega-3-triglycerides	30 (4.5)	61 (9.2)	91 (13.8)
Agents acting on the renin-angiotensin system	**198 (30.0)**	**263 (39.8)**	**461 (69.7)**
Perindopril	61 (9.2)	35 (5.3)	96 (14.5)
Irbesartan	33 (5.0)	51 (7.7)	84 (12.7)
Ramipril	42 (6.4)	38 (5.7)	80 (12.1)
Analgesics	**167 (25.3)**	**290 (43.9)**	**457 (69.1)**
Paracetamol	142 (21.5)	252 (38.1)	394 (59.6)
Codeine, combinations excl. psycholeptics	27 (4.1)	45 (6.8)	72 (10.9)
Oxycodone	12 (1.8)	23 (3.5)	35 (5.3)
Antithrombotic agents	**212 (32.1)**	**244 (36.9)**	**456 (69.0)**
Acetylsalicylic acid	129 (19.5)	155 (23.4)	284 (43.0)
Warfarin	59 (8.9)	58 (8.8)	117 (17.7)
Clopidogrel	50 (7.6)	49 (7.4)	99 (15.0)
Drugs for acid related disorders	**155 (23.4)**	**229 (34.6)**	**384 (58.1)**
Esomeprazole	48 (7.3)	67 (10.1)	115 (17.4)
Omeprazole	34 (5.1)	64 (9.7)	98 (14.8)
Pantoprazole	31 (4.7)	40 (6.1)	71 (10.7)
Cardiac therapy	**142 (21.5)**	**150 (22.7)**	**292 (44.2)**
Glyceryl trinitrate	66 (10.0)	72 (10.9)	138 (20.9)
Digoxin	42 (6.4)	44 (6.7)	86 (13.0)
Isosorbide mononitrate	32 (4.8)	23 (3.5)	55 (8.3)
Diuretics	**87 (13.2)**	**142 (21.5)**	**229 (34.6)**
Furosemide	69 (10.4)	105 (15.9)	174 (26.3)
Spironolactone	20 (3.0)	16 (2.4)	36 (5.4)
Indapamide	10 (1.5)	24 (3.6)	34 (5.1)
Drugs for obstructive airway diseases	**88 (13.3)**	**135 (20.4)**	**223 (33.7)**
Salbutamol	57 (8.6)	90 (13.6)	147 (22.2)
Salmeterol and other drugs for obstructive airway diseases	37 (5.6)	55 (8.3)	92 (13.9)
Tiotropium bromide	39 (5.9)	40 (6.1)	79 (12.0)
Calcium channel blockers	**87 (13.2)**	**135 (20.4)**	**222 (33.6)**
Amlodipine	26 (3.9)	44 (6.7)	70 (10.6)
Diltiazem	21 (3.2)	29 (4.4)	50 (7.6)
Lercanidipine	12 (1.8)	27 (4.1)	39 (5.9)
Beta blocking agents	**100 (15.1)**	**117 (17.7)**	**217 (32.8)**
Metoprolol	45 (6.8)	53 (8.0)	98 (14.8)
Atenolol	31 (4.7)	49 (7.4)	80 (12.1)
Carvedilol	10 (1.5)	8 (1.2)	18 (2.7)
Psychoanaleptics	**80 (12.1)**	**129 (19.5)**	**209 (31.6)**
Amitriptyline	13 (2.0)	33 (5.0)	46 (7.0)
Sertraline	11 (1.7)	19 (2.9)	30 (4.5)
Mirtazapine	11 (1.7)	13 (2.0)	24 (3.6)

ATC LEVEL 2 MEDICATION GROUP MOST FREQUENT INDIVIDUAL MEDICATIONS (ATC LEVEL 5)	NUMBER OF PATIENTS TAKING (% OF TOTAL) MALES N=278 (42.1)	FEMALES N=383 (57.9)	TOTAL N=661
Antiinflammatory and antirheumatic products	**70 (10.6)**	**130 (19.7)**	**200 (30.3)**
Glucosamine	28 (4.2)	72 (10.9)	100 (15.1)
Meloxicam	15 (2.3)	36 (5.4)	51 (7.7)
Celecoxib	9 (1.4)	18 (2.7)	27 (4.1)
Drugs used in diabetes	**94 (14.2)**	**98 (14.8)**	**192 (29.0)**
Metformin	67 (10.1)	66 (10.0)	133 (20.1)
Gliclazide	38 (5.7)	47 (7.1)	85 (12.9)
Insulin (human)	10 (1.5)	14 (2.1)	24 (3.6)
Mineral supplements	**46 (7.0)**	**135 (20.4)**	**181 (27.4)**
Calcium carbonate	20 (3.0)	84 (12.7)	104 (15.7)
Potassium chloride	14 (2.1)	35 (5.3)	49 (7.4)
Magnesium (different salts in combination)	2 (0.3)	7 (1.1)	9 (1.4)
Vitamins	**48 (7.3)**	**133 (20.1)**	**181 (27.4)**
Colecalciferol	21 (3.2)	67 (10.1)	88 (13.3)
Multivitamins and other minerals, incl. combinations	13 (2.0)	34 (5.1)	47 (7.1)
Ascorbic acid (vit C)	6 (0.9)	14 (2.1)	20 (3.0)
Ophthalmologicals	**58 (8.8)**	**120 (18.2)**	**178 (26.9)**
Artificial tears and other indifferent preparations	37 (5.6)	77 (11.6)	114 (17.2)
Latanoprost	13 (2.0)	15 (2.3)	28 (4.2)
Timolol	3 (0.5)	9 (1.4)	12 (1.8)
Laxatives	**72 (10.9)**	**102 (15.4)**	**174 (26.3)**
Senna glycosides, combinations	31 (4.7)	44 (6.7)	75 (11.3)
Senna glycosides	7 (1.1)	21 (3.2)	28 (4.2)
Lactulose	11 (1.7)	16 (2.4)	27 (4.1)
Psycholeptics	**60 (9.1)**	**106 (16.0)**	**166 (25.1)**
Temazepam	27 (4.1)	55 (8.3)	82 (12.4)
Oxazepam	6 (0.9)	31 (4.7)	37 (5.6)
Diazepam	16 (2.4)	15 (2.3)	31 (4.7)
Antianaemic preparations	**46 (7.0)**	**86 (13.0)**	**132 (20.0)**
Hydroxocobalamin	19 (2.9)	26 (3.9)	45 (6.8)
Folic acid	13 (2.0)	30 (4.5)	43 (6.5)
Ferrous sulfate	5 (0.8)	19 (2.9)	24 (3.6)
Corticosteroids, dermatological preparations	**47 (7.1)**	**78 (11.8)**	**125 (18.9)**
Betamethasone	24 (3.6)	31 (4.7)	55 (8.3)
Mometasone	15 (2.3)	27 (4.1)	42 (6.4)
Hydrocortisone	9 (1.4)	8 (1.2)	17 (2.6)

5.3.3 Indication for HMR referral

The frequencies of the reasons why each patient was referred for a HMR are shown in Table 64. Given the high number of medications taken by the majority of the patients, it is unsurprising that the most frequently listed indication for the HMR was taking 5

or more regular medications. Many of these referrals contained additional comments requesting that the pharmacists assess the safety of the patient's drug regimen in terms of drug interactions and educate the patient as to the indications for each of their medications. Interestingly, no clear reason for a HMR was documented in approximately one third of the HMR referrals.

TABLE 64 - REASONS FOR HMR DOCUMENTED IN REFERRALS

INDICATION FOR HMR REFERRAL	NUMBER (%) OF PATIENTS
Currently taking 5 or more regular medications	366 (55.4)
Taking more than 12 doses of medication per day	85 (12.9)
Medication with a narrow therapeutic index or medications requiring therapeutic monitoring	73 (11.0)
Patient having difficulty managing their own medicines because of literacy or language difficulties, dexterity problems or impaired sight, confusion/dementia or other cognitive difficulties	61 (9.2)
Sub-optimal response to treatment with medicines	61 (9.2)
Significant changes made to medication treatment regimen in the last 3 months	55 (8.3)
Suspected non-compliance or inability to manage medication-related therapeutic devices	51 (7.7)
Recent discharge from a facility / hospital (in the last 4 weeks)	37 (5.6)
Symptoms suggestive of an adverse drug reaction	30 (4.5)
Attending a number of different doctors, both general practitioners and specialists	17 (2.6)
Other*	9 (1.4)
HMR required for the DVA DAA program	39 (5.9)
No reason specified	217 (32.8)

* Included requests such as "*Check for drug interactions*", "*Alleviate patient anxiety regarding medications*" and "*Explain asthma action plan*"
Note that many referrals listed more than one reason for the HMR

Many HMRs listed several criteria as being applicable to the patient - more than one reason for the HMR referral was documented in 241 (36.5%) of the HMRs. The maximum number of reasons for the HMR was 8; however, the GPs indicated that more than 3 criteria applied to only 30 patients. It may be that the referrals which listed many criteria did so because of computer default settings as opposed to the patients actually filling the criteria.

5.4 Drug-related problems identified

The pharmacists documented 2323 actual or potential DRPs in the HMR reports, equating to 3.5 (SD ±1.8, range 0-13) DRPs per HMR. No DRPs were documented in eighteen HMRs (2.7%).

5.4.1 Type of DRPs

The frequency of the DRPs identified according to the D.O.C.U.M.E.N.T. classification system are shown in Table 65. The most frequently identified type of DRP involved *Untreated indications*, which accounted for 27% of all DRPs identified. More pointedly, 76% of all patients were documented by the pharmacists as requiring either intensification of their current therapy or additional therapy.

TABLE 65 - NUMBER OF DRPS IDENTIFIED CLASSIFIED ACCORDING TO D.O.C.U.M.E.N.T. SYSTEM

DRP TYPE DRP SUBTYPE	NUMBER (%) OF TOTAL DRPS	 PATIENTS
Drug selection	**511 (22.0)**	**423 (64.0)**
Drug interaction	189 (8.1)	142 (21.5)
Contraindications apparent	135 (5.8)	115 (17.4)
Unnecessary therapy/no apparent current indication	132 (5.7)	111 (16.8)
Duplication	36 (1.5)	36 (5.4)
Other drug selection problem	15 (0.6)	15 (2.3)
Wrong dosage form	3 (0.1)	3 (0.5)
Wrong drug	1 (0.0)	1 (0.2)
Over or underdose prescribed	**198 (8.5)**	**185 (28.0)**
Dose too high	117 (5.0)	107 (16.2)
Dose too low	45 (1.9)	43 (6.5)
Other dose problem	36 (1.5)	35 (5.3)
Compliance & concordance	**321 (13.8)**	**298 (45.1)**
Taking too little	133 (5.7)	119 (18.0)
Other compliance problem	119 (5.1)	112 (16.9)
Difficulty using dosage form	40 (1.7)	38 (5.7)
Patient using out of date medication	16 (0.7)	16 (2.4)
Taking too much	13 (0.6)	13 (2.0)
Untreated indications	**638 (27.5)**	**500 (75.6)**
Condition not adequately treated	373 (16.1)	288 (43.6)
Therapy required	262 (11.3)	209 (31.6)
Other untreated indication problem	3 (0.1)	3 (0.5)
Monitoring	**238 (10.2)**	**196 (29.7)**
Laboratory monitoring	216 (9.3)	174 (26.3)
Non-laboratory monitoring	19 (0.8)	19 (2.9)
Other monitoring problem	3 (0.1)	3 (0.5)
Education or information	**44 (1.9)**	**40 (6.1)**
Disease management or advice	15 (0.6)	11 (1.7)
Confusion about therapy	9 (0.4)	9 (1.4)
Demonstration of device	9 (0.4)	9 (1.4)
Patient drug information request	6 (0.3)	6 (0.9)
Other education or information problem	5 (0.2)	5 (0.8)
Non-clinical	**55 (2.4)**	**55 (8.3)**
Other non-clinical problem	14 (0.6)	14 (2.1)
Dietary problem	13 (0.6)	13 (2.0)
Smoking problem	13 (0.6)	13 (2.0)
Weight management problem	11 (0.5)	11 (1.7)
Alcohol problem	4 (0.2)	4 (0.6)
Toxicity or adverse reaction	**318 (13.7)**	**261 (39.5)**
Toxicity evident	247 (10.6)	194 (29.3)
Toxicity caused by drug interaction	39 (1.7)	36 (5.4)
Toxicity caused by dose	27 (1.2)	26 (3.9)
Other toxicity/adverse effect problem	5 (0.2)	5 (0.8)
TOTAL	**2323 (100.0)**	**(n=661)**

Drug- selection issues, such as potentially interacting drugs or patients taking medications that were potentially contraindicated, were also frequently identified (22% of DRPs identified). *Drug interactions* were the most common DRP of this type, with pharmacists documenting more than one in five patients as taking a potentially problematic combination of drugs. Approximately 17% of patients were taking a drug to which they had a potential contraindication.

The pharmacists documented approximately 40% of the patients as experiencing a suspected adverse effect from one or more of their drugs. The majority of these were due to single drugs (247 DRPs, 78%), although drug interactions were thought to be responsible for 12% of all ADEs. DRPs involving *Compliance and concordance* issues were documented in 45% of the HMR reports, with these patients most commonly taking medications too infrequently. Few patients were exceeding their directed doses (13 DRPs, 2% of patients).

It is notable that the proportion of DRPs related to *Education or information* appeared to be low, with only 6% of patients documented as requiring further information. However, these figures only represented data contained in the HMR reports. In consideration that one of the goals of HMRs is to ensure patients are knowledgeable about their drugs and medical conditions, it is likely that substantially more education was provided during the HMR interview than these figures suggest. The survey finding that most of the participating pharmacists place significant emphasis on patient education (Section 5.2.4) would also suggest that this was the case.

To characterise the DRPs, they were examined according to the associated medical conditions and drugs. The following sections present the results of this analysis.

5.4.2 Medical conditions associated with DRPs

Of the 2323 DRPs documented in the HMR reports, 1386 were specifically associated with either causing or resulting from a medical condition or symptom. Table 66 shows the class of medical conditions (using ICPC2-PLUS chapter grouping) associated with each subtype of DRP. As a single DRP may have been associated with more than one condition or symptom, 1554 DRPs are included in the table. The data presented provides some indication as to the medical conditions frequently targeted in the

pharmacists' interventions, discussed below. This data is presented in more detail in Table 150 (Appendix XXII) which shows the individual medical conditions (using ICPC2-PLUS disease terms) associated with the DRPs.

TABLE 66 - NUMBER OF DRPS DOCUMENTED BY PHARMACISTS IN HMR REPORTS GROUPED ACCORDING TO ASSOCIATED MEDICAL CONDITIONS

	NUMBER (% OF DRP TYPE) OF DRPS ACCORDING TO ASSOCIATED MEDICAL CONDITIONS GROUPS (GROUPED BY ICPC2-PLUS CHAPTERS)																
DRP TYPE **DRP SUBTYPE**	BLOOD, BLOOD FORM ORGANS & IMMUNE MECHANISM	CARDIOVASCULAR	DIGESTIVE	EAR	ENDOCRINE, METABOLIC AND NUTRITIONAL	EYE	FEMALE GENITAL	GENERAL & UNSPECIFIED	MALE GENITAL	MUSCULOSKELETAL	NEUROLOGICAL	PSYCHOLOGICAL	RESPIRATORY	SKIN	SOCIAL PROBLEMS	UROLOGICAL	TOTAL
Drug selection	**2 (0.9)**	**31 (13.9)**	**31 (13.9)**	**0**	**33 (14.8)**	**3 (1.3)**	**2 (0.9)**	**22 (9.9)**	**1 (0.4)**	**21 (9.4)**	**10 (4.5)**	**18 (8.1)**	**16 (7.2)**	**2 (0.9)**	**0**	**31 (13.9)**	**223 (100)**
Duplication	0	3 (1.3)	2 (0.9)	0	4 (1.8)	0	0	0	0	2 (0.9)	0	0	2 (0.9)	0	0	0	**13 (5.8)**
Drug interaction	1 (0.4)	5 (2.2)	5 (2.2)	0	7 (3.1)	0	0	11 (4.9)	0	6 (2.7)	3 (1.3)	0	0	1 (0.4)	0	6 (2.7)	**45 (20.2)**
Wrong drug	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1 (0.4)	**1 (0.4)**
Wrong dosage form	0	0	0	0	0	0	0	0	0	0	0	0	2 (0.9)	0	0	0	**2 (0.9)**
Unnecessary therapy/no apparent current indication	1 (0.4)	5 (2.2)	14 (6.3)	0	10 (4.5)	0	0	5 (2.2)	1 (0.4)	3 (1.3)	1 (0.4)	8 (3.6)	4 (1.8)	1 (0.4)	0	3 (1.3)	**56 (25.1)**
Contraindications apparent	0	15 (6.7)	10 (4.5)	0	10 (4.5)	3 (1.3)	2 (0.9)	6 (2.7)	0	10 (4.5)	6 (2.7)	9 (4.0)	8 (3.6)	0	0	20 (9.0)	**99 (44.4)**
Other drug selection problem	0	3 (1.3)	0	0	2 (0.9)	0	0	0	0	0	0	1 (0.4)	0	0	0	1 (0.4)	**7 (3.1)**
Over or under-dose prescribed	**0**	**14 (11.5)**	**22 (18.0)**	**1 (0.8)**	**29 (23.8)**	**0**	**0**	**3 (2.5)**	**0**	**16 (13.1)**	**4 (3.3)**	**7 (5.7)**	**4 (3.3)**	**0**	**0**	**22 (18.0)**	**122 (100)**
Dose too high	0	5 (4.1)	17 (13.9)	1 (0.8)	13 (10.7)	0	0	0	0	7 (5.7)	2 (1.6)	3 (2.5)	3 (2.5)	0	0	19 (15.6)	**70 (57.4)**
Dose too low	0	7 (5.7)	3 (2.5)	0	10 (8.2)	0	0	0	0	7 (5.7)	0	2 (1.6)	0	0	0	2 (1.6)	**31 (25.4)**

DRP Type DRP subtype	Number (% of DRP type) of DRPs according to associated medical conditions groups (grouped by ICPC2-PLUS chapters) Blood, Blood form Organs & Immune Mechanism	Cardiovascular	Digestive	Ear	Endocrine, Metabolic and Nutritional	Eye	Female Genital	General & Unspecified	Male Genital	Musculoskeletal	Neurological	Psychological	Respiratory	Skin	Social Problems	Urological	Total
Other dose problem	0	2 (1.6)	2 (1.6)	0	6 (4.9)	0	0	3 (2.5)	0	2 (1.6)	2 (1.6)	2 (1.6)	1 (0.8)	0	0	1 (0.8)	**21 (17.2)**
Compliance and concordance	**1 (1.0)**	**18 (18.4)**	**12 (12.2)**	**0**	**12 (12.2)**	**5 (5.1)**	**0**	**4 (4.1)**	**0**	**7 (7.1)**	**2 (2.0)**	**5 (5.1)**	**27 (27.6)**	**1 (1.0)**	**2 (2.0)**	**2 (2.0)**	**98 (100)**
Taking too little	1 (1.0)	12 (12.2)	3 (3.1)	0	8 (8.2)	4 (4.1)	0	1 (1.0)	0	3 (3.1)	1 (1.0)	2 (2.0)	19 (19.4)	1 (1.0)	2 (2.0)	1 (1.0)	**58 (59.2)**
Taking too much	0	0	1 (1.0)	0	2 (2.0)	0	0	2 (2.0)	0	0	0	1 (1.0)	2 (2.0)	0	0	1 (1.0)	**9 (9.2)**
Difficulty using dosage form	0	2 (2.0)	8 (8.2)	0	0	1 (1.0)	0	0	0	0	0	1 (1.0)	6 (6.1)	0	0	0	**18 (18.4)**
Patient using out of date medication	0	1 (1.0)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	**1 (1.0)**
Other compliance problem	0	3 (3.1)	0	0	2 (2.0)	0	0	1 (1.0)	0	4 (4.1)	1 (1.0)	1 (1.0)	0	0	0	0	**12 (12.2)**
Untreated indications	**1 (0.2)**	**99 (17.3)**	**52 (9.1)**	**0**	**104 (18.2)**	**5 (0.9)**	**1 (0.2)**	**94 (16.4)**	**1 (0.2)**	**106 (18.5)**	**13 (2.3)**	**28 (4.9)**	**41 (7.2)**	**8 (1.4)**	**0**	**20 (3.5)**	**573 (100)**
Condition not adequately treated	0	69 (12.0)	29 (5.1)	0	51 (8.9)	2 (0.3)	1 (0.2)	78 (13.6)	1 (0.2)	74 (12.9)	6 (1.0)	19 (3.3)	29 (5.1)	4 (0.7)	0	6 (1.0)	**369 (64.4)**
Therapy required	1 (0.2)	29 (5.1)	23 (4.0)	0	52 (9.1)	3 (0.5)	0	16 (2.8)	0	32 (5.6)	7 (1.2)	9 (1.6)	11 (1.9)	4 (0.7)	0	13 (2.3)	**200 (34.9)**
Other untreated indication problem	0	1 (0.2)	0	0	1 (0.2)	0	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	**4 (0.7)**
Monitoring	3 (2.8)	10 (9.4)	2 (1.9)	0	44 (41.5)	0	0	13 (12.3)	1 (0.9)	13 (12.3)	3 (2.8)	4 (3.8)	1 (0.9)	0	0	12 (11.3)	**106 (100)**
Laboratory monitoring	3 (2.8)	4 (3.8)	2 (1.9)	0	35 (33.0)	0	0	12 (11.3)	0	13 (12.3)	3 (2.8)	3 (2.8)	1 (0.9)	0	0	12 (11.3)	**88 (83.0)**

DRP Type DRP subtype	Number (% of DRP type) of DRPs according to associated medical conditions groups (grouped by ICPC2-PLUS chapters)																
	Blood, Blood form Organs & Immune Mechanism	Cardiovascular	Digestive	Ear	Endocrine, Metabolic and Nutritional	Eye	Female Genital	General & Unspecified	Male Genital	Musculoskeletal	Neurological	Psychological	Respiratory	Skin	Social Problems	Urological	Total
Non-laboratory monitoring	0	6 (5.7)	0	0	8 (7.5)	0	0	1 (0.9)	1 (0.9)	0	0	1 (0.9)	0	0	0	0	**17 (16.0)**
Other monitoring problem	0	0	0	0	1 (0.9)	0	0	0	0	0	0	0	0	0	0	0	**1 (0.9)**
Education or information	**0**	**0**	**0**	**0**	**4 (21.1)**	**0**	**0**	**1 (5.3)**	**0**	**3 (15.8)**	**0**	**0**	**9 (47.4)**	**1 (5.3)**	**0**	**1 (5.3)**	**19 (100)**
Patient drug information request	0	0	0	0	0	0	0	0	0	1 (5.3)	0	0	0	0	0	0	**1 (5.3)**
Confusion about therapy	0	0	0	0	0	0	0	0	0	0	0	0	3 (15.8)	0	0	0	**3 (15.8)**
Demonstration of device	0	0	0	0	1 (5.3)	0	0	0	0	1 (5.3)	0	0	2 (10.5)	0	0	0	**4 (21.1)**
Disease management or advice	0	0	0	0	3 (15.8)	0	0	1 (5.3)	0	1 (5.3)	0	0	3 (15.8)	1 (5.3)	0	1 (5.3)	**10 (52.6)**
Other education or information problem	0	0	0	0	0	0	0	0	0	0	0	0	1 (5.3)	0	0	0	**1 (5.3)**
Non-clinical	**0**	**5 (11.9)**	**3 (7.1)**	**0**	**13 (31.0)**	**0**	**1 (2.4)**	**4 (9.5)**	**0**	**0**	**0**	**11 (26.2)**	**1 (2.4)**	**0**	**0**	**4 (9.5)**	**42 (100)**
Weight management problem	0	1 (2.4)	1 (2.4)	0	9 (21.4)	0	0	0	0	0	0	0	0	0	0	1 (2.4)	**12 (28.6)**
Dietary problem	0	2 (4.8)	0	0	4 (9.5)	0	0	1 (2.4)	0	0	0	0	0	0	0	2 (4.8)	**9 (21.4)**
Smoking problem	0	1 (2.4)	0	0	0	0	0	0	0	0	0	11 (26.2)	1 (2.4)	0	0	0	**13 (31.0)**

DRP Type / DRP subtype	Number (% of DRP type) of DRPs according to associated medical conditions groups (grouped by ICPC2-PLUS chapters)																
	Blood, Blood form Organs & Immune Mechanism	Cardiovascular	Digestive	Ear	Endocrine, Metabolic and Nutritional	Eye	Female Genital	General & Unspecified	Male Genital	Musculoskeletal	Neurological	Psychological	Respiratory	Skin	Social Problems	Urological	Total
Alcohol problem	0	0	1 (2.4)	0	0	0	0	1 (2.4)	0	0	0	0	0	0	0	0	**2 (4.8)**
Other non-clinical problem	0	1 (2.4)	1 (2.4)	0	0	0	1 (2.4)	2 (4.8)	0	0	0	0	0	0	0	1 (2.4)	**6 (14.3)**
Toxicity or adverse reaction	**11 (3.0)**	**36 (9.7)**	**98 (26.4)**	**1 (0.3)**	**27 (7.3)**	**5 (1.3)**	**0**	**33 (8.9)**	**0**	**31 (8.4)**	**38 (10.2)**	**21 (5.7)**	**32 (8.6)**	**19 (5.1)**	**0**	**19 (5.1)**	**371 (100)**
Toxicity caused by dose	0	5 (1.3)	13 (3.5)	0	6 (1.6)	0	0	2 (0.5)	0	5 (1.3)	3 (0.8)	1 (0.3)	0	0	0	2 (0.5)	**37 (10.0)**
Toxicity caused by drug interaction	3 (0.8)	5 (1.3)	6 (1.6)	0	2 (0.5)	1 (0.3)	0	4 (1.1)	0	2 (0.5)	5 (1.3)	0	2 (0.5)	1 (0.3)	0	1 (0.3)	**32 (8.6)**
Toxicity evident	8 (2.2)	26 (7.0)	78 (21.0)	1 (0.3)	19 (5.1)	4 (1.1)	0	27 (7.3)	0	24 (6.5)	30 (8.1)	20 (5.4)	30 (8.1)	18 (4.9)	0	16 (4.3)	**301 (81.1)**
Other toxicity/adverse effect problem	0	0	1 (0.3)	0	0	0	0	0	0	0	0	0	0	0	0	0	**1 (0.3)**
Total	**18 (1.2)**	**213 (13.7)**	**220 (14.2)**	**2 (0.1)**	**266 (17.1)**	**18 (1.2)**	**4 (0.3)**	**174 (11.2)**	**3 (0.2)**	**197 (12.7)**	**70 (4.5)**	**94 (6.0)**	**131 (8.4)**	**31 (2.0)**	**2 (0.1)**	**111 (7.1)**	**1554 (100)**

The DRPs related to *Untreated indications* involved several body systems, those most frequently involved being *General and unspecified* and *Musculoskeletal conditions*. In actuality, there was considerable overlap between these two classes as the most common individual condition was pain resulting from osteoarthritis. Depending upon how the DRP was presented in the HMR report, it was documented as either *Pain* (for example, "the patient is in pain") or *Osteoarthritis* ("the patient's osteoarthritis is poorly controlled"). *Untreated indication* DRPs involving the *Cardiovascular* system were also frequently identified. In contrast, there was a much broader range of medical conditions associated with *Drug selection* DRPs. The most frequently occurring DRP of this type involved patients with renal dysfunction taking drugs contraindicated in renal (*Urological* conditions) or cardiovascular diseases. In terms of medications without clear indications, *Digestive* system disorders were the most frequently identified DRP type.

The body system most frequently associated with DRPs was the endocrine system. The most common types of DRPs involving this system were *Untreated indications* and *Monitoring* issues, which accounted for over half of endocrine-related DRPs (138 DRPs, 52%). Type II diabetes mellitus was the condition most frequently associated with DRPs; it was involved in 121 (5%) of all DRPs identified by the pharmacists. Given its prevalence in the study sample (approximately one third of patients were diabetic), as well as the variety of drugs used to treat diabetes and the complexities involved in managing it, it is unsurprising that this condition was associated with a broad range of DRP subtypes. Approximately one third of the DRPs associated with diabetes (48 DRPs, 40% of all diabetes-related DRPs) involved suboptimal management; the remaining DRPs were of 19 other subtypes.

5.4.3 Drugs associated with DRPs

5.4.3.1 Overview

For each DRP documented by the pharmacists in the HMR reports, the drug/s associated with it were also recorded. Of the 2323 DRPs identified by the pharmacists, 1799 were specifically associated with one or more drugs (mean 1.1 drug per DRP ± 0.9, range 0 to 8). Table 67 shows the drug classes (ATC level 1 coding) associated with each subtype of DRP. The proportion of patients taking at least one drug of each class is also presented to indicate the prevalence of each drug class in the DRPs. As a

single DRP may have been associated with more than drug, 2691 DRPs are included in the table. As with Table 66, the data presented outlines the drug types frequently targeted in the pharmacists' interventions. Further detail is presented in Table 151 (Appendix XIX) which lists the DRPs resulting from drug types (ATC level 3 coding) as opposed to the broad drug groups shown in Table 67.

TABLE 67 - NUMBER OF DRPS DOCUMENTED BY PHARMACISTS IN HMR REPORTS GROUPED ACCORDING TO ASSOCIATED DRUG GROUPS (ATC LEVEL ONE)

	NUMBER (% OF SUBTYPE) OF DRPS ACCORDING TO DRUG GROUPS (GROUPED BY ATC LEVEL ONE HEADINGS)														
DRP TYPE **DRP SUBTYPE**	ALIMENTARY TRACT AND METABOLISM	ANTIINFECTIVES FOR SYSTEMIC USE	ANTINEOPLASTIC AND IMMUNOMODULATING AGENTS	ANTIPARASITIC PRODUCTS, INSECTICIDES AND REPELLENTS	BLOOD AND BLOOD FORMING ORGANS	CARDIOVASCULAR SYSTEM	DERMATOLOGICALS	GENITO URINARY SYSTEM AND SEX HORMONES	MUSCULO-SKELETAL SYSTEM	NERVOUS SYSTEM	RESPIRATORY SYSTEM	SENSORY ORGANS	SYSTEMIC HORMONAL PREPARATIONS, EXCLUDING SEX HORMONES AND INSULINS	VARIOUS	
NUMBER (%) PATIENTS TAKING	**569 (86.1)**	**60 (9.1)**	**37 (5.6)**	**21 (3.2)**	**504 (76.2)**	**637 (96.4)**	**142 (21.5)**	**81 (12.3)**	**322 (48.7)**	**529 (80.0)**	**259 (39.2)**	**183 (27.7)**	**135 (20.4)**	**19 (2.9)**	**TOTAL**
Drug selection	**131 (15.4)**	**13 (1.5)**	**11 (1.3)**	**9 (1.1)**	**111 (13.1)**	**255 (30.0)**	**1 (0.1)**	**11 (1.3)**	**105 (12.4)**	**142 (16.7)**	**36 (4.2)**	**8 (0.9)**	**17 (2.0)**	**0**	**850 (100)**
Duplication	10 (1.2)	0	0	0	15 (1.8)	13 (1.5)	0	0	9 (1.1)	6 (0.7)	14 (1.6)	2 (0.2)	2 (0.2)	0	**71 (8.4)**
Drug interaction	33 (3.9)	3 (0.4)	9 (1.1)	1 (0.1)	75 (8.8)	184 (21.6)	0	4 (0.5)	49 (5.8)	45 (5.3)	5 (0.6)	1 (0.1)	13 (1.5)	0	**422 (49.6)**
Wrong drug	0	1 (0.1)	0	0	0	0	0	0	0	0	0	0	0	0	**1 (0.1)**
Wrong dosage form	0	0	0	0	0	1 (0.1)	0	0	0	0	2 (0.2)	0	0	0	**3 (0.4)**
Unnecessary therapy/no apparent current indication	54 (6.4)	4 (0.5)	0	0	18 (2.1)	26 (3.1)	0	4 (0.5)	15 (1.8)	25 (2.9)	11 (1.3)	1 (0.1)	1 (0.1)	0	**159 (18.7)**
Contraindications apparent	33 (3.9)	5 (0.6)	2 (0.2)	8 (0.9)	3 (0.4)	22 (2.6)	1 (0.1)	3 (0.4)	32 (3.8)	61 (7.2)	2 (0.2)	3 (0.4)	0	0	**175 (20.6)**
Other drug selection problem	1 (0.1)	0	0	0	0	9 (1.1)	0	0	0	5 (0.6)	2 (0.2)	1 (0.1)	1 (0.1)	0	**19 (2.2)**
Over or underdose prescribed	**69 (30.7)**	**2 (0.9)**	**4 (1.8)**	**0**	**9 (4.0)**	**64 (28.4)**	**0**	**3 (1.3)**	**30 (13.3)**	**31 (13.8)**	**5 (2.2)**	**4 (1.8)**	**4 (1.8)**	**0**	**225 (100)**

	Number (% of subtype) of DRPs according to drug groups (grouped by ATC level one headings)														
DRP type **DRP subtype**	Alimentary tract and metabolism	Antiinfectives for systemic use	Antineoplastic and immunomodulating agents	Antiparasitic products, insecticides and repellents	Blood and blood forming organs	Cardiovascular system	Dermatologicals	Genito urinary system and sex hormones	Musculo-skeletal system	Nervous system	Respiratory system	Sensory organs	Systemic hormonal preparations, excluding sex hormones and insulins	Various	
Number (%) patients taking	**569 (86.1)**	**60 (9.1)**	**37 (5.6)**	**21 (3.2)**	**504 (76.2)**	**637 (96.4)**	**142 (21.5)**	**81 (12.3)**	**322 (48.7)**	**529 (80.0)**	**259 (39.2)**	**183 (27.7)**	**135 (20.4)**	**19 (2.9)**	**Total**
Dose too high	45 (20.0)	1 (0.4)	2 (0.9)	0	4 (1.8)	36 (16.0)	0	2 (0.9)	24 (10.7)	16 (7.1)	4 (1.8)	3 (1.3)	2 (0.9)	0	**139 (61.8)**
Dose too low	11 (4.9)	1 (0.4)	2 (0.9)	0	3 (1.3)	19 (8.4)	0	0	5 (2.2)	2 (0.9)	0	1 (0.4)	1 (0.4)	0	**45 (20.0)**
Other dose problem	13 (5.8)	0	0	0	2 (0.9)	9 (4.0)	0	1 (0.4)	1 (0.4)	13 (5.8)	1 (0.4)	0	1 (0.4)	0	**41 (18.2)**
Compliance	**40 (14.8)**	**0**	**0**	**0**	**18 (6.7)**	**78 (28.9)**	**5 (1.9)**	**4 (1.5)**	**12 (4.4)**	**31 (11.5)**	**69 (25.6)**	**7 (2.6)**	**6 (2.2)**	**0**	**270 (100)**
Taking too little	18 (6.7)	0	0	0	12 (4.4)	33 (12.2)	4 (1.5)	0	6 (2.2)	10 (3.7)	32 (11.9)	5 (1.9)	0	0	**120 (44.4)**
Taking too much	4 (1.5)	0	0	0	1 (0.4)	0	0	1 (0.4)	1 (0.4)	4 (1.5)	3 (1.1)	0	2 (0.7)	0	**16 (5.9)**
Difficulty using dosage form	7 (2.6)	0	0	0	0	8 (3.0)	0	2 (0.7)	0	5 (1.9)	29 (10.7)	0	0	0	**51 (18.9)**
Patient using out of date medication	0	0	0	0	1 (0.4)	11 (4.1)	1 (0.4)	0	0	0	1 (0.4)	2 (0.7)	0	0	**16 (5.9)**
Other compliance problem	11 (4.1)	0	0	0	4 (1.5)	26 (9.6)	0	1 (0.4)	5 (1.9)	12 (4.4)	4 (1.5)	0	4 (1.5)	0	**67 (24.8)**
Untreated indications	**89 (16.2)**	**12 (2.2)**	**6 (1.1)**	**0**	**13 (2.4)**	**145 (26.3)**	**1 (0.2)**	**4 (0.7)**	**41 (7.4)**	**189 (34.3)**	**37 (6.7)**	**2 (0.4)**	**11 (2.0)**	**1 (0.2)**	**551 (100)**
Condition not adequately	73 (13.2)	0	6 (1.1)	0	6 (1.1)	130 (23.6)	1 (0.2)	4 (0.7)	37 (6.7)	177 (32.1)	35 (6.4)	2 (0.4)	2 (0.4)	0	**473 (85.8)**

	Number (% of subtype) of DRPs according to drug groups (grouped by ATC level one headings)														
DRP type **DRP subtype**	Alimentary tract and metabolism	Antiinfectives for systemic use	Antineoplastic and immunomodulating agents	Antiparasitic products, insecticides and repellents	Blood and blood forming organs	Cardiovascular system	Dermatologicals	Genito urinary system and sex hormones	Musculo-skeletal system	Nervous system	Respiratory system	Sensory organs	Systemic hormonal preparations, excluding sex hormones and insulins	Various	
Number (%) patients taking	**569 (86.1)**	**60 (9.1)**	**37 (5.6)**	**21 (3.2)**	**504 (76.2)**	**637 (96.4)**	**142 (21.5)**	**81 (12.3)**	**322 (48.7)**	**529 (80.0)**	**259 (39.2)**	**183 (27.7)**	**135 (20.4)**	**19 (2.9)**	**Total**
treated															
Therapy required	16 (2.9)	12 (2.2)	0	0	7 (1.3)	15 (2.7)	0	0	4 (0.7)	12 (2.2)	2 (0.4)	0	9 (1.6)	1 (0.2)	**78 (14.2)**
Monitoring	**80 (33.3)**	**1 (0.4)**	**5 (2.1)**	**0**	**8 (3.3)**	**109 (45.4)**	**1 (0.4)**	**3 (1.3)**	**7 (2.9)**	**13 (5.4)**	**6 (2.5)**	**0**	**7 (2.9)**	**0**	**240 (100)**
Laboratory monitoring	79 (32.9)	1 (0.4)	5 (2.1)	0	7 (2.9)	100 (41.7)	1 (0.4)	3 (1.3)	7 (2.9)	12 (5.0)	6 (2.5)	0	7 (2.9)	0	**228 (95.0)**
Non-laboratory monitoring	1 (0.4)	0	0	0	1 (0.4)	8 (3.3)	0	0	0	0	0	0	0	0	**10 (4.2)**
Other monitoring problem	0	0	0	0	0	1 (0.4)	0	0	0	1 (0.4)	0	0	0	0	**2 (0.8)**
Education or information	**1 (3.1)**	**0**	**0**	**0**	**3 (9.4)**	**5 (15.6)**	**1 (3.1)**	**1 (3.1)**	**2 (6.3)**	**4 (12.5)**	**15 (46.9)**	**0**	**0**	**0**	**32 (100)**
Patient drug information request	0	0	0	0	2 (6.3)	0	0	1 (3.1)	0	1 (3.1)	0	0	0	0	**4 (12.5)**
Confusion about therapy	1 (3.1)	0	0	0	1 (3.1)	1 (3.1)	1 (3.1)	0	1 (3.1)	2 (6.3)	6 (18.8)	0	0	0	**13 (40.6)**
Demonstration of device	0	0	0	0	0	0	0	0	0	0	7 (21.9)	0	0	0	**7 (21.9)**
Disease management or advice	0	0	0	0	0	0	0	0	0	0	2 (6.3)	0	0	0	**2 (6.3)**

	Number (% of subtype) of DRPs according to drug groups (grouped by ATC level one headings)														
DRP type **DRP subtype**	Alimentary tract and metabolism	Antiinfectives for systemic use	Antineoplastic and immunomodulating agents	Antiparasitic products, insecticides and repellents	Blood and blood forming organs	Cardiovascular system	Dermatologicals	Genito urinary system and sex hormones	Musculo-skeletal system	Nervous system	Respiratory system	Sensory organs	Systemic hormonal preparations, excluding sex hormones and insulins	Various	
Number (%) patients taking	**569 (86.1)**	**60 (9.1)**	**37 (5.6)**	**21 (3.2)**	**504 (76.2)**	**637 (96.4)**	**142 (21.5)**	**81 (12.3)**	**322 (48.7)**	**529 (80.0)**	**259 (39.2)**	**183 (27.7)**	**135 (20.4)**	**19 (2.9)**	**Total**
Other education or information problem	0	0	0	0	0	4 (12.5)	0	0	1 (3.1)	1 (3.1)	0	0	0	0	**6 (18.8)**
Non-clinical	**2 (11.1)**	**0**	**0**	**0**	**9 (50.0)**	**6 (33.3)**	**0**	**0**	**0**	**1 (5.6)**	**0**	**0**	**0**	**0**	**18 (100)**
Dietary problem	0	0	0	0	2 (11.1)	1 (5.6)	0	0	0	0	0	0	0	0	**3 (16.7)**
Smoking problem	0	0	0	0	0	1 (5.6)	0	0	0	0	0	0	0	0	**1 (5.6)**
Alcohol problem	2 (11.1)	0	0	0	2 (11.1)	2 (11.1)	0	0	0	0	0	0	0	0	**6 (33.3)**
Other non-clinical problem	0	0	0	0	5 (27.8)	2 (11.1)	0	0	0	1 (5.6)	0	0	0	0	**8 (44.4)**
Toxicity or adverse reaction	**75 (14.9)**	**2 (0.4)**	**7 (1.4)**	**3 (0.6)**	**46 (9.1)**	**216 (42.8)**	**1 (0.2)**	**7 (1.4)**	**31 (6.1)**	**84 (16.6)**	**17 (3.4)**	**0**	**16 (3.2)**	**0**	**505 (100)**
Toxicity caused by dose	10 (2.0)	0	0	0	2 (0.4)	15 (3.0)	0	0	0	5 (1.0)	0	0	4 (0.8)	0	**36 (7.1)**
Toxicity caused by drug interaction	9 (1.8)	0	0	0	15 (3.0)	37 (7.3)	1 (0.2)	1 (0.2)	2 (0.4)	15 (3.0)	1 (0.2)	0	1 (0.2)	0	**82 (16.2)**
Toxicity evident	52 (10.3)	2 (0.4)	7 (1.4)	3 (0.6)	28 (5.5)	163 (32.3)	0	6 (1.2)	28 (5.5)	64 (12.7)	16 (3.2)	0	11 (2.2)	0	**380 (75.2)**

	Number (% of subtype) of DRPs according to drug groups (grouped by ATC level one headings)														
DRP type **DRP subtype**	**Alimentary tract and metabolism**	**Antiinfectives for systemic use**	**Antineoplastic and immunomodulating agents**	**Antiparasitic products, insecticides and repellents**	**Blood and blood forming organs**	**Cardiovascular system**	**Dermatologicals**	**Genito urinary system and sex hormones**	**Musculo-skeletal system**	**Nervous system**	**Respiratory system**	**Sensory organs**	**Systemic hormonal preparations, excluding sex hormones and insulins**	**Various**	
Number (%) patients taking	**569 (86.1)**	**60 (9.1)**	**37 (5.6)**	**21 (3.2)**	**504 (76.2)**	**637 (96.4)**	**142 (21.5)**	**81 (12.3)**	**322 (48.7)**	**529 (80.0)**	**259 (39.2)**	**183 (27.7)**	**135 (20.4)**	**19 (2.9)**	**Total**
Other toxicity/adverse effect problem	4 (0.8)	0	0	0	1 (0.2)	1 (0.2)	0	0	1 (0.2)	0	0	0	0	0	**7 (1.4)**
Total	**487 (18.1)**	**30 (1.1)**	**33 (1.2)**	**12 (0.4)**	**217 (8.1)**	**878 (32.6)**	**10 (0.4)**	**33 (1.2)**	**228 (8.5)**	**495 (18.4)**	**185 (6.9)**	**21 (0.8)**	**61 (2.3)**	**1 (0.0)**	**2691 (100)**

The drug group most frequently involved in the DRPs was *Cardiovascular* medications. These drugs were often involved in various subtypes of DRPs, with *Drug interactions*, *Condition not adequately treated* and several *Toxicity or adverse reaction* DRP subtypes being the most common. These results were somewhat expected in consideration of the high proportion of patients with cardiovascular conditions and taking drugs in this class. The drug class next most frequently associated with DRPs involved drugs for nervous system disorders. Similarly to cardiovascular drugs, the DRP subtype with which these drugs were most frequently involved was *Untreated indications.* However, a greater proportion of *Contraindications apparent* were associated with these drugs than other types, primarily due to concerns regarding benzodiazepine and tricyclic antidepressant use in the elderly.

Drugs for *Alimentary tract and metabolism disorders* were frequently involved in DRPs relating to both undertreatment and overtreatment. This drug class was the second most frequently involved in DRPs relating to inadequate therapeutic monitoring, with proton pump inhibitors and anti-diabetic agents accounting for 64 of the 79 DRPs of this type (81%).

5.4.3.2 DRPs involving drugs of specific interest

To further investigate the characteristics of the DRPs, several drugs of specific interest were identified based on them being of narrow therapeutic index or frequently involved in DRPs. The following drugs or drug groups were examined in terms of the types of DRPs with which they were involved:

- Warfarin (narrow therapeutic index),
- Digoxin (narrow therapeutic index),
- Proton pump inhibitors (frequently involved),
- Paracetamol (frequently involved),
- HMG-CoA reductase inhibitors (frequently involved),
- Antiplatelet agents (frequently involved),
- Angiotensin-converting enzyme (ACE) inhibitors and angiotensin 2 receptor antagonists (frequently involved),
- Non-steroidal anti-inflammatory drugs (frequently involved), and
- Diuretics (frequently involved).

Four other drugs commonly considered to be of narrow therapeutic indices- methotrexate, lithium, phenytoin and theophylline - are not included in the following discussion as the numbers of patients taking them were small (17, four, four and two patients, respectively).

5.4.3.2.1 Warfarin

Warfarin-related DRPs were documented in 51 of the 117 patients taking warfarin (ATC level 5 code B01AA03). The subtypes of warfarin-related DRPs are shown in Table 68. The most common subtypes of these DRPs involved drug interactions, which accounted for approximately half of the warfarin-related DRPs (31 out of 63 DRPs). Eleven DRPs involved patients displaying signs of warfarin-related toxicity, most frequently minor bleeding or elevated internationalised normalised ratios (INRs).

TABLE 68 - SUBTYPES OF DRPS INVOLVING WARFARIN IN PATIENTS TAKING WARFARIN

TYPE DESCRIPTION	SUBTYPE DESCRIPTION	NUMBER (% OF TOTAL NUMBER OF DRP SUBTYPE)
Drug selection	Duplication	2 (5.6)
Drug selection	Drug interaction	26 (13.8)
Drug selection	Unnecessary therapy/no apparent current indication	4 (3.0)
Drug selection	Contraindications apparent	2 (1.5)
Over or underdose prescribed	Dose too high	1 (0.9)
Over or underdose prescribed	Other Dose Problem	1 (2.8)
Compliance	Taking too little	1 (0.8)
Compliance	Other Compliance Problem	3 (2.5)
Untreated indications	Condition not adequately treated	1 (0.3)
Untreated indications	Therapy required	2 (0.8)
Monitoring	Laboratory Monitoring	4 (1.9)
Education or Information	Patient drug information request	2 (33.3)
Non-clinical	Dietary problem	2 (15.4)
Non-clinical	Other non-clinical problem	1 (7.1)
Toxicity or Adverse reaction	Toxicity caused by dose	1 (3.7)
Toxicity or Adverse reaction	Toxicity caused by drug interaction	5 (12.8)
Toxicity or Adverse reaction	Toxicity evident	5 (2.0)
Total (n=2323)		**63 (2.7)**

5.4.3.2.2 Digoxin

Of the 86 patients taking digoxin (ATC level 5 code C01AA05), 49 were documented with digoxin-related DRPs (Table 69). Similarly to warfarin, drug interactions were the most commonly identified subtype of digoxin-related DRPs. However, it appeared that DRPs relating to inadequate monitoring of digoxin therapy were more frequently identified than DRPs involving inadequate monitoring of warfarin.

TABLE 69 - SUBTYPES OF DRPS INVOLVING DIGOXIN IN PATIENTS TAKING DIGOXIN

TYPE DESCRIPTION	SUBTYPE DESCRIPTION	NUMBER (% OF TOTAL NUMBER OF DRP SUBTYPE)
Drug selection	Duplication	1 (2.8)
Drug selection	Drug interaction	14 (7.4)
Over or underdose prescribed	Dose too high	4 (3.4)
Over or underdose prescribed	Dose too low	1 (2.2)
Over or underdose prescribed	Other Dose Problem	2 (5.6)
Compliance	Taking too little	2 (1.5)
Untreated indications	Condition not adequately treated	2 (0.5)
Monitoring	Laboratory Monitoring	13 (6.0)
Monitoring	Other Monitoring Problem	1 (33.3)
Toxicity or Adverse reaction	Toxicity caused by dose	2 (7.4)
Toxicity or Adverse reaction	Toxicity caused by drug interaction	4 (10.3)
Toxicity or Adverse reaction	Toxicity evident	7 (2.8)
Total (n=2323)		**53 (2.3)**

5.4.3.2.3 Proton pump inhibitors

Three hundred and thirty seven patients were taking proton pump inhibitors (ATC level 4 code A02BC), of whom 137 were documented as having DRPs involving proton pump inhibitor therapy. Interestingly, the most frequently identified DRP involving these drugs related to inadequate monitoring of therapy (Table 70), primarily vitamin B_{12} levels. A similarly high proportion of DRPs involving these drugs related to patients taking doses above those recommended by guidelines, or taking a proton pump inhibitor in the absence of a clear indication for it. This may have been influenced by publications addressing the appropriate use of these drugs that were

distributed by the National Prescribing Service and Veterans' MATES program around the time of the study.[255, 256]

TABLE 70 - SUBTYPES OF DRPS INVOLVING PROTON PUMP INHIBITORS IN PATIENTS TAKING THEM

TYPE DESCRIPTION	SUBTYPE DESCRIPTION	NUMBER (% OF TOTAL NUMBER OF DRP SUBTYPE)
Drug selection	Duplication	3 (8.3)
Drug selection	Drug interaction	7 (3.7)
Drug selection	Unnecessary therapy/no apparent current indication	30 (22.7)
Drug selection	Contraindications apparent	4 (3.0)
Over or underdose prescribed	Dose too high	23 (19.7)
Over or underdose prescribed	Dose too low	1 (2.2)
Over or underdose prescribed	Other Dose Problem	1 (2.8)
Compliance	Taking too little	3 (2.3)
Compliance	Taking too much	2 (15.4)
Compliance	Difficulty using dosage form	4 (10.0)
Compliance	Other Compliance Problem	3 (2.5)
Untreated indications	Condition not adequately treated	13 (3.5)
Untreated indications	Therapy required	2 (0.8)
Monitoring	Laboratory Monitoring	38 (17.6)
Toxicity or Adverse reaction	Toxicity caused by dose	1 (3.7)
Toxicity or Adverse reaction	Toxicity caused by drug interaction	4 (10.3)
Toxicity or Adverse reaction	Toxicity evident	23 (9.3)
Toxicity or Adverse reaction	Other Toxicity/Adverse Effect problem	2 (0.1)
Total (n=2323)		**164 (7.1)**

5.4.3.2.4 Paracetamol

Of the 402 patients taking paracetamol (ATC level 4 code N02BE), 122 were documented as having DRPs involving their paracetamol therapy. Almost all of these DRPs involved patients taking paracetamol to manage pain without adequate pain relief (Table 71). The small number of other DRP types is understandable, given the relative safety of paracetamol.

TABLE 71 - SUBTYPES OF DRPS INVOLVING PARACETAMOL IN PATIENTS TAKING PARACETAMOL

TYPE DESCRIPTION	SUBTYPE DESCRIPTION	NUMBER (% OF TOTAL NUMBER OF DRP SUBTYPE)
Drug selection	Drug interaction	8 (4.2)
Drug selection	Contraindications apparent	3 (2.2)
Over or underdose prescribed	Dose too high	3 (2.6)
Over or underdose prescribed	Dose too low	1 (2.2)
Over or underdose prescribed	Other Dose Problem	1 (2.8)
Compliance	Taking too little	3 (2.3)
Compliance	Taking too much	1 (7.7)
Compliance	Difficulty using dosage form	2 (5.0)
Compliance	Other Compliance Problem	3 (2.5)
Untreated indications	Condition not adequately treated	93 (24.9)
Untreated indications	Therapy required	1 (0.4)
Monitoring	Laboratory Monitoring	2 (0.9)
Non-clinical	Other non-clinical problem	1 (7.1)
Toxicity or Adverse reaction	Toxicity caused by dose	1 (3.7)
Toxicity or Adverse reaction	Toxicity caused by drug interaction	2 (5.1)
Toxicity or Adverse reaction	Toxicity evident	1 (0.4)
Total (n=2323)		**126 (5.4)**

5.4.3.2.5 HMG-CoA reductase inhibitors

Four hundred patients were taking HMG-CoA reductase inhibitors (ATC level 4 code C10AA), and 108 of them were documented as having DRPs involving their HMG-CoA reductase inhibitor therapy (Table 72). Most frequently, these DRPs involved *Drug interactions*, *Adverse reactions* (primarily myalgia), inadequate *Laboratory monitoring* and insufficient management of dyslipidaemia. The frequency of the subtypes of DRPs involving HMG-CoA reductase inhibitors is shown in Table 72.

TABLE 72 - SUBTYPES OF DRPS INVOLVING HMG CO-A REDUCTASE INHIBITORS IN PATIENTS TAKING THEM

TYPE DESCRIPTION	SUBTYPE DESCRIPTION	NUMBER (% OF TOTAL NUMBER OF DRP SUBTYPE)
Drug selection	Duplication	2 (5.6)
Drug selection	Drug interaction	26 (13.8)
Drug selection	Unnecessary therapy/no apparent current indication	3 (2.3)
Over or underdose prescribed	Dose too high	7 (6.0)
Over or underdose prescribed	Dose too low	1 (2.2)
Over or underdose prescribed	Other Dose Problem	3 (8.3)
Compliance	Taking too little	4 (3.0)
Compliance	Difficulty using dosage form	2 (5.0)
Compliance	Other Compliance Problem	3 (2.5)
Untreated indications	Condition not adequately treated	22 (5.9)
Monitoring	Laboratory Monitoring	20 (9.3)
Education or Information	Other Education or Information Problem	1 (20.0)
Non-clinical	Other non-clinical problem	1 (7.1)
Toxicity or Adverse reaction	Toxicity caused by dose	2 (7.4)
Toxicity or Adverse reaction	Toxicity caused by drug interaction	2 (5.1)
Toxicity or Adverse reaction	Toxicity evident	24 (9.7)
Total (n=2323)		**123 (5.3)**

5.4.3.2.6 Antiplatelet agents

Of the 365 patients taking antiplatelet agents (ATC level 4 code B01AC), 94 were documented as having DRPs involving their antiplatelet therapy. The most common subtype of DRP associated with antiplatelet drugs involved drug interactions, particularly involving dual antiplatelet therapy and combinations with anticoagulant drugs (Table 73). Twenty seven adverse reactions were attributed to antiplatelet drugs, primarily related to symptoms of minor bleeding.

TABLE 73 - SUBTYPES OF DRPS INVOLVING ANTIPLATELET AGENTS IN PATIENTS TAKING THEM

TYPE DESCRIPTION	SUBTYPE DESCRIPTION	NUMBER (% OF TOTAL NUMBER OF DRP SUBTYPE)
Drug selection	Duplication	9 (25.0)
Drug selection	Drug interaction	35 (18.5)
Drug selection	Unnecessary therapy/no apparent current indication	7 (5.3)
Drug selection	Contraindications apparent	1 (0.7)
Over or underdose prescribed	Dose too high	2 (1.7)
Compliance	Taking too little	9 (6.8)
Compliance	Taking too much	1 (7.7)
Compliance	Other Compliance Problem	1 (0.8)
Untreated indications	Condition not adequately treated	2 (0.5)
Untreated indications	Therapy required	4 (1.5)
Monitoring	Laboratory Monitoring	1 (0.5)
Non-clinical	Alcohol problem	2 (50.0)
Non-clinical	Other non-clinical problem	2 (14.3)
Toxicity or Adverse reaction	Toxicity caused by drug interaction	7 (17.9)
Toxicity or Adverse reaction	Toxicity evident	19 (7.7)
Toxicity or Adverse reaction	Other Toxicity/Adverse Effect problem	1 (20.0)
Total (n=2323)		**103 (4.4)**

5.4.3.2.7 ACE inhibitors and angiotensin 2 receptor antagonists

Of the 461 patients taking ACE inhibitors and angiotensin II receptor antagonists (ATC level 2 code C09), 168 were documented with DRPs involving this therapy. DRPs involving these drugs were most frequently *Drug interactions*, which accounted for approximately 30% of all the DRPs of this subtype identified in the study (Table 74). Most interactions involved co-administration of drugs that would affect potassium levels (such as diuretics) or cause renal toxicity (for example, NSAIDs). These drugs were also frequently associated with DRPs relating to undertreated cardiovascular disease, which is understandable in consideration of the high number of DRPs of this subtype (see section 5.4.1). Adverse reactions were often attributed to this drug group, the most common of which was cough associated with ACE inhibitors.

TABLE 74 - SUBTYPES OF DRPS INVOLVING DRUGS WORKING ON THE RENIN-ANGIOTENSIN SYSTEM IN PATIENTS TAKING THEM

TYPE DESCRIPTION	SUBTYPE DESCRIPTION	NUMBER (% OF TOTAL NUMBER OF DRP SUBTYPE)
Drug selection	Duplication	1 (2.8)
Drug selection	Drug interaction	55 (29.1)
Drug selection	Unnecessary therapy/no apparent current indication	3 (2.3)
Drug selection	Contraindications apparent	4 (3.0)
Drug selection	Other drug selection problem	2 (13.3)
Over or underdose prescribed	Dose too high	6 (5.1)
Over or underdose prescribed	Dose too low	7 (15.6)
Compliance	Taking too little	2 (1.5)
Compliance	Other Compliance Problem	5 (4.2)
Untreated indications	Condition not adequately treated	36 (9.7)
Untreated indications	Therapy required	3 (1.1)
Monitoring	Laboratory Monitoring	28 (13.0)
Monitoring	Non-Laboratory monitoring	3 (15.8)
Education or Information	Other Education or Information Problem	1 (20.0)
Non-clinical	Dietary problem	1 (7.7)
Toxicity or Adverse reaction	Toxicity caused by dose	2 (7.4)
Toxicity or Adverse reaction	Toxicity caused by drug interaction	5 (12.8)
Toxicity or Adverse reaction	Toxicity evident	35 (14.2)
Total (n=2323)		**199 (8.6)**

5.4.3.2.8 Non-steroidal anti-inflammatory drugs

Of the 199 patients taking NSAIDs (ATC level 3 code M01A), 103 were documented as having DRPs involving this therapy. These drugs were associated with a range of DRP subtypes (Table 75), the most frequent being *Drug interactions*. Interactions commonly identified included potential renal toxicity with ACE inhibitors, angiotensin II antagonists and diuretics, and increased risk of gastrointestinal bleeding in combination with low-dose aspirin. Additionally, NSAIDs were the drug group most frequently identified as being contraindicated, accounting for 18% of all DRPs of this type.

TABLE 75 - SUBTYPES OF DRPS INVOLVING NON-STEROIDAL ANTI-INFLAMMATORY DRUGS IN PATIENTS TAKING THEM

TYPE DESCRIPTION	SUBTYPE DESCRIPTION	NUMBER (% OF TOTAL NUMBER OF DRP SUBTYPE)
Drug selection	Duplication	3 (8.3)
Drug selection	Drug interaction	40 (21.2)
Drug selection	Unnecessary therapy/no apparent current indication	3 (2.3)
Drug selection	Contraindications apparent	25 (18.5)
Over or underdose prescribed	Dose too high	5 (4.3)
Over or underdose prescribed	Dose too low	4 (8.9)
Compliance	Other Compliance Problem	1 (0.8)
Untreated indications	Condition not adequately treated	16 (4.3)
Monitoring	Laboratory Monitoring	1 (0.5)
Education or Information	Confusion about therapy	1 (11.1)
Education or Information	Other Education or Information Problem	1 (20.0)
Toxicity or Adverse reaction	Toxicity caused by drug interaction	2 (5.1)
Toxicity or Adverse reaction	Toxicity evident	12 (4.9)
Toxicity or Adverse reaction	Other Toxicity/Adverse Effect problem	1 (20.0)
Total (n=2323)		**115 (5.0)**

5.4.3.2.9 Diuretics

Eighty nine of the 229 patients taking diuretics (ATC level 2 code C03) were documented as having DRPs involving their diuretic therapy. The DRPs associated with diuretic usage are shown in Table 76. The most common DRP related to diuretic use involved *Drug interactions*, frequently in association with NSAIDs and ACE inhibitors/ angiotensin II antagonists, as previously discussed.

TABLE 76 - SUBTYPES OF DRPS INVOLVING DIURETICS IN PATIENTS TAKING THEM

TYPE DESCRIPTION	SUBTYPE DESCRIPTION	NUMBER (% OF TOTAL NUMBER OF DRP SUBTYPE)
Drug selection	Duplication	2 (5.6)
Drug selection	Drug interaction	33 (17.5)
Drug selection	Unnecessary therapy/no apparent current indication	7 (5.3)
Drug selection	Contraindications apparent	2 (1.5)
Over or underdose prescribed	Dose too high	6 (5.1)
Over or underdose prescribed	Dose too low	1 (2.2)
Over or underdose prescribed	Other Dose Problem	1 (2.8)
Compliance	Taking too little	4 (3.0)
Compliance	Other Compliance Problem	3 (2.5)
Untreated indications	Condition not adequately treated	7 (1.9)
Untreated indications	Therapy required	3 (1.1)
Monitoring	Laboratory Monitoring	13 (6.0)
Toxicity or Adverse reaction	Toxicity caused by dose	4 (14.8)
Toxicity or Adverse reaction	Toxicity caused by drug interaction	8 (20.5)
Toxicity or Adverse reaction	Toxicity evident	17 (6.9)
Total (n=2323)		**111 (4.8)**

5.4.4 Overall DRP characteristics

It was possible to incorporate the drug and medical condition data with the DRP subtypes to characterise in detail the DRPs. The results of this analysis is shown in Table 77, which lists the 20 most frequently occurring DRPs according to the drugs and conditions involved in the DRP. The high prevalence of suboptimal therapy is again evident in this table, with 13 of the 20 DRPs involving conditions inadequately treated. The two most frequently identified ADRs involved reasonably minor symptoms of ACE-inhibitor induced cough and pedal oedema associated with calcium channel blockers. Interestingly, the most frequently identified DRP involving a lack of monitoring was vitamin B_{12} levels in patients taking proton pump inhibitors.

TABLE 77 - THE 20 MOST FREQUENTLY OCCURRING DRPS ACCORDING TO THE DRUGS AND CONDITIONS INVOLVED

DRP SUBTYPE	DRUG INVOLVED (ATC LEVEL 2)	CONDITION INVOLVED	NUMBER OF DRPS (% OF PATIENTS EXPERIENCING)
Condition not adequately treated	Analgesics	General symptom/complaint, other*	99 (15.0)
Condition not adequately treated	Agents acting on the renin-angiotensin system	Hypertension, uncomplicated	37 (5.6)
Condition not adequately treated	Lipid modifying agents	Lipid disorder	26 (3.9)
Condition not adequately treated	Drugs used in diabetes	Diabetes, non-insulin dependent	25 (3.8)
Condition not adequately treated	Analgesics	Osteoarthrosis, other	19 (2.9)
Condition not adequately treated	Drugs for obstructive airway diseases	Chronic obstructive pulmonary disease	15 (2.3)
Condition not adequately treated	Beta blocking agents	Hypertension, uncomplicated	15 (2.3)
Condition not adequately treated	Drugs for treatment of bone diseases	Osteoporosis	14 (2.1)
Condition not adequately treated	Calcium channel blockers	Hypertension, uncomplicated	14 (2.1)
Toxicity evident	Agents acting on the renin-angiotensin system	Cough	13 (2.0)
Condition not adequately treated	Laxatives	Constipation	12 (1.8)
Dose too high	Drugs for acid related disorders	Oesophagus disease	11 (1.7)
Condition not adequately treated	Drugs for acid related disorders	Oesophagus disease	11 (1.7)
Condition not adequately treated	Antiinflammatory and antirheumatic products	General symptom/complaint, other*	11 (1.7)
Laboratory Monitoring	Drugs for acid related disorders	Vitamin/nutritional deficiency	9 (1.4)
Contraindications apparent	Drugs used in diabetes	Diabetes, non-insulin dependent	9 (1.4)
Condition not adequately treated	Analgesics	Back symptom/complaint	9 (1.4)
Taking too little	Drugs for obstructive airway diseases	Asthma	9 (1.4)
Toxicity evident	Calcium channel blockers	Swollen ankles/oedema	8 (1.2)
Drug interaction	Agents acting on the renin-angiotensin system	Abnormal result/investigation not otherwise specified**	8 (1.2)

* pain **renal insufficiency

It is apparent from the data presented in this section that the pharmacists documented a large number of potential DRPs in the HMRs. Furthermore, there were many different types of DRP identified, involving a broad range of drugs and medical conditions. However, as discussed in section 1.1.2 of this thesis, the identification of

DRPs is only part of the HMR process; DRPs must be resolved or managed to prevent undesirable outcomes. The following section describes the recommendations made by the pharmacists to resolve or prevent the DRPs from occurring.

5.4.5 Recommendations made

The recommendations made to resolve each DRP were classified according to the DOCUMENT classification system. The pharmacists made 2610 recommendations to resolve the DRPs, equating to approximately one recommendation per DRP. Descriptive statistics for the number of recommendations made per DRP and per HMR are shown in Table 78. No recommendation was made to resolve 117 DRPs (5.0%) in 20 HMRs (3.0%), of which no DRPs were identified in all but two HMRs.

TABLE 78 - DESCRIPTIVE STATISTICS FOR NUMBER OF RECOMMENDATIONS MADE PER DRP AND PER HMR

PARAMETER	PER DRP	PER HMR
Mean ± SD [range]	1.2 ± 0.5	3.9 ± 2.3
Median [interquartile range]	1 [1 - 1]	4 [2 - 5]
Range	0 - 4	0 - 17

The frequencies of the types and subtypes of recommendations made by the pharmacists are shown in Table 79. The most frequently made type of recommendation involved changes to a patient's drug therapy, with at least one change to therapy recommended for 577 patients (87%). Notably, the number of recommendations made to commence a new drug or increase the dose of an existing drug was substantially higher than the number of recommendations made to reduce the dose or cease existing medications (684 recommendations, 26.2% - versus 488 recommendations, 18.7%).

Recommendations for additional monitoring were also made frequently, with these types of recommendations made for about half of the patients. The most commonly made subtype of all recommendations was to perform laboratory monitoring, such as electrolyte levels or therapeutic drug monitoring. It is possible that more monitoring

was recommended than the *Non-laboratory monitoring* figure suggests, since patients may perform much of this monitoring themselves (for example, blood pressure and blood glucose levels).

TABLE 79 - RECOMMENDATIONS MADE TO RESOLVE DRPS

RECOMMENDATION TYPE SUBTYPE	NUMBER (%) OF TOTAL RECOMMENDATIONS	NUMBER (%) OF PATIENTS (N=661)*
Monitoring	**570 (21.8)**	**356 (53.9)**
Laboratory monitoring	470 (18.0)	314 (47.5)
Non-laboratory monitoring	100 (3.8)	92 (13.9)
For follow-up	**180 (6.9)**	**134 (20.3)**
Follow-up by prescriber	133 (5.1)	113 (17.1)
Follow-up by another	47 (1.8)	38 (5.7)
Provision of education or information	**277 (10.6)**	**218 (33.0)**
Patient/carer education	163 (6.2)	134 (20.3)
Prescriber information	13 (0.5)	13 (2.0)
Compliance assistance	101 (3.9)	95 (14.4)
Drug or dosage modification	**1583 (60.7)**	**577 (87.3)**
Dose increase	226 (8.7)	192 (29.0)
Dose decrease	191 (7.3)	158 (23.9)
Drug cease	297 (11.4)	226 (34.2)
Drug start	458 (17.5)	300 (45.4)
Formulation change	62 (2.4)	57 (8.6)
Dose schedule change	72 (2.8)	71 (10.7)
Drug switch	272 (10.4)	212 (32.1)
Other therapy change	5 (0.2)	5 (0.8)
TOTAL	**2610 (100)**	
No recommendation	**117 DRPs (5.0)**	
No recommendation necessary	11 DRPs (0.5)	
No recommendation made	106 DRPs (4.6)	

*Totals for each type of recommendation are less than totals for subtypes of recommendations as one patient may have had several subtypes of recommendations made

To characterise the relationship between the recommendations and the DRPs, the recommendations were analysed according to the DRP types for which they were made. The number of recommendations made to resolve each type of DRP is shown in Table 80, and provides some insight into the ways in which the pharmacists attempted to resolve the DRPs.

TABLE 80 - NUMBER OF RECOMMENDATIONS MADE TO RESOLVE EACH DRP SUBTYPE

	NUMBER (% SUBTYPE) OF RECOMMENDATIONS MADE TO RESOLVE DRPS ACCORDING TO DRP SUBTYPES																	
	DRUG OR DOSAGE MODIFICATION								MONITORING		PROVISION OF EDUCATION OR INFORMATION			FOR FOLLOW-UP			NO RECOMMENDATION	
DRP TYPE **DRP SUBTYPE**	DRUG CEASE	DRUG START	DRUG SWITCH	DOSE DECREASE	DOSE INCREASE	DOSE SCHEDULE CHANGE	FORMULATION CHANGE	OTHER THERAPY CHANGE	LABORATORY MONITORING	NON-LABORATORY MONITORING	COMPLIANCE ASSISTANCE	PATIENT/CARER EDUCATION	PRESCRIBER INFORMATION	FOLLOW-UP BY ANOTHER	FOLLOW-UP BY PRESCRIBER	TOTAL	NO RECOMMENDATION NECESSARY	NO RECOMMENDATION MADE
Drug selection	**191 (34.7)**	**20 (3.6)**	**96 (17.4)**	**36 (6.5)**	**13 (2.4)**	**12 (2.2)**	**5 (0.9)**	**1 (0.2)**	**105 (19.1)**	**42 (7.6)**	**0 (0.0)**	**10 (1.8)**	**3 (0.5)**	**5 (0.9)**	**12 (2.2)**	**551 (100)**	**5**	**27**
Duplication	25 (4.5)	0	2 (0.4)	3 (0.5)	0	1 (0.2)	0	1 (0.2)	3 (0.5)	0	0	0	0	1 (0.2)	1 (0.2)	37 (6.7)	0	2
Drug interaction	30 (5.4)	9 (1.6)	20 (3.6)	5 (0.9)	4 (0.7)	9 (1.6)	1 (0.2)	0	76 (13.8)	33 (6.0)	0	4 (0.7)	1 (0.2)	0	3 (0.5)	195 (35.4)	4	13
Wrong drug	1 (0.2)	0	1 (0.2)	0	0	0	0	0	0	0	0	0	0	0	0	2 (0.4)	0	0
Wrong dosage form	0	1 (0.2)	0	0	0	0	3 (0.5)	0	0	0	0	0	0	0	0	4 (0.7)	0	0
Unnecessary therapy/ no apparent current indication	**90 (16.3)**	**2 (0.4)**	**8 (1.5)**	**16 (2.9)**	**3 (0.5)**	**0**	**0**	**0**	**12 (2.2)**	**1 (0.2)**	**0**	**0**	**1 (0.2)**	**1 (0.2)**	**3 (0.5)**	**137 (24.9)**	**0**	**4**
Contraindications apparent	42 (7.6)	8 (1.5)	58 (10.5)	12 (2.2)	6 (1.1)	2 (0.4)	0	0	13 (2.4)	7 (1.3)	0	5 (0.9)	1 (0.2)	3 (0.5)	4 (0.7)	161 (29.2)	1	7
Other drug selection problem	3 (0.5)	0	7 (1.3)	0	0	0	1 (0.2)	0	1 (0.2)	1 (0.2)	0	1 (0.2)	0	0	1 (0.2)	15 (2.7)	0	1

DRP type / DRP subtype	Number (% subtype) of recommendations made to resolve DRPs according to DRP subtypes																
	Drug or dosage modification								Monitoring		Provision of education or information			For follow-up			No recommendation
	Drug cease	Drug start	Drug switch	Dose decrease	Dose increase	Dose schedule change	Formulation change	Other therapy change	Laboratory monitoring	Non-laboratory monitoring	Compliance assistance	Patient/carer education	Prescriber information	Follow-up by another	Follow-up by prescriber	Total	No recommendation necessary	No recommendation made
Over or under-dose prescribed	**21 (9.3)**	**7 (3.1)**	**13 (5.8)**	**80 (35.6)**	**40 (17.8)**	**26 (11.6)**	**0 (0.0)**	**1 (0.4)**	**21 (9.3)**	**3 (1.3)**	**0 (0.0)**	**2 (0.9)**	**1 (0.4)**	**3 (1.3)**	**7 (3.1)**	**225 (100)**	**0**	**3**
Dose too high	19 (8.4)	6 (2.7)	11 (4.9)	77 (34.2)	4 (1.8)	2 (0.9)	0	0	11 (4.9)	1 (0.4)	0	1 (0.4)	1 (0.4)	0	1 (0.4)	134 (59.6)	0	2
Dose too low	1 (0.4)	1 (0.4)	1 (0.4)	1 (0.4)	36 (16.0)	0	0	1 (0.4)	7 (3.1)	2 (0.9)	0	0	0	3 (1.3)	0	53 (23.6)	0	1
Other dose problem	1 (0.4)	0	1 (0.4)	2 (0.9)	0	24 (10.7)	0	0	3 (1.3)	0	0	1 (0.4)	0	0	6 (2.7)	38 (16.9)	0	0
Compliance and concordance	**11 (3.3)**	**8 (2.4)**	**19 (5.6)**	**5 (1.5)**	**13 (3.8)**	**13 (3.8)**	**38 (11.2)**	**2 (0.6)**	**11 (3.3)**	**1 (0.3)**	**93 (27.5)**	**63 (18.6)**	**0 (0.0)**	**8 (2.4)**	**53 (15.7)**	**338 (100)**	**0**	**8**
Taking too little	7 (2.1)	7 (2.1)	6 (1.8)	2 (0.6)	11 (3.3)	7 (2.1)	5 (1.5)	0	8 (2.4)	1 (0.3)	31 (9.2)	44 (13.0)	0	4 (1.2)	14 (4.1)	147 (43.5)	0	4
Taking too much	1 (0.3)	1 (0.3)	0	2 (0.6)	0	0	0	0	2 (0.6)	0	2 (0.6)	4 (1.2)	0	0	2 (0.6)	14 (4.1)	0	1
Difficulty using dosage form	1 (0.3)	0	5 (1.5)	0	0	0	17 (5.0)	1 (0.3)	0	0	11 (3.3)	5 (1.5)	0	1 (0.3)	1 (0.3)	42 (12.4)	0	1
Patient using out of date medication	0	0	1 (0.3)	1 (0.3)	0	0	1 (0.3)	0	0	0	1 (0.3)	4 (1.2)	0	0	8 (2.4)	16 (4.7)	0	0

DRP type / DRP subtype	Number (% subtype) of recommendations made to resolve DRPs according to DRP subtypes																
	Drug or dosage modification								Monitoring		Provision of education or information			For follow-up			No recommendation	
	Drug cease	Drug start	Drug switch	Dose decrease	Dose increase	Dose schedule change	Formulation change	Other therapy change	Laboratory monitoring	Non-laboratory monitoring	Compliance assistance	Patient/carer education	Prescriber information	Follow-up by another	Follow-up by prescriber	Total	No recommendation necessary	No recommendation made
Other compliance problem	2 (0.6)	0	7 (2.1)	0	2 (0.6)	6 (1.8)	15 (4.4)	1 (0.3)	1 (0.3)	0	48 (14.2)	6 (1.8)	0	3 (0.9)	28 (8.3)	119 (35.2)	0	2
Untreated indications	**12 (1.6)**	**365 (47.3)**	**55 (7.1)**	**8 (1.0)**	**152 (19.7)**	**11 (1.4)**	**9 (1.2)**	**0 (0.0)**	**76 (9.9)**	**10 (1.3)**	**5 (0.6)**	**26 (3.4)**	**1 (0.1)**	**14 (1.8)**	**27 (3.5)**	**771 (100)**	**3**	**12**
Condition not adequately treated	12 (1.6)	168 (21.8)	50 (6.5)	6 (0.8)	149 (19.3)	11 (1.4)	8 (1.0)	0	31 (4.0)	6 (0.8)	5 (0.6)	17 (2.2)	0	7 (0.9)	9 (1.2)	479 (62.1)	0	7
Therapy required	0	197 (25.6)	5 (0.6)	2 (0.3)	3 (0.4)	0	1 (0.1)	0	43 (5.6)	4 (0.5)	0	9 (1.2)	1 (0.1)	6 (0.8)	17 (2.2)	288 (37.4)	3	5
Other untreated indication problem	0	0	0	0	0	0	0	0	2 (0.3)	0	0	0	0	1 (0.1)	1 (0.1)	4 (0.5)		
Monitoring	**3 (1.1)**	**8 (3.1)**	**3 (1.1)**	**4 (1.5)**	**0 (0.0)**	**2 (0.8)**	**0 (0.0)**	**0 (0.0)**	**201 (76.7)**	**33 (12.6)**	**0 (0.0)**	**1 (0.4)**	**3 (1.1)**	**3 (1.1)**	**1 (0.4)**	**262 (100)**	**0**	**3**
Laboratory monitoring	3 (1.1)	8 (3.1)	3 (1.1)	4 (1.5)	0	0	0	0	200 (76.3)	15 (5.7)	0	1 (0.4)	2 (0.8)	1 (0.4)	1 (0.4)	238 (90.8)	0	3
Non-laboratory monitoring	0	0	0	0	0	1 (0.4)	0	0	1 (0.4)	18 (6.9)	0	0	0	1 (0.4)	0	21 (8.0)	0	0
Other monitoring problem	0	0	0	0	0	1 (0.4)	0	0	0	0	0	0	1 (0.4)	1 (0.4)	0	3 (1.1)	0	0

DRP type / DRP subtype	Number (% subtype) of recommendations made to resolve DRPs according to DRP subtypes																	
	Drug or dosage modification								Monitoring		Provision of education or information			For follow-up			No recommendation	
	Drug cease	Drug start	Drug switch	Dose decrease	Dose increase	Dose schedule change	Formulation change	Other therapy change	Laboratory monitoring	Non-laboratory monitoring	Compliance assistance	Patient/carer education	Prescriber information	Follow-up by another	Follow-up by prescriber	Total	No recommendation necessary	No recommendation made
Education or information	**1 (2.2)**	**0 (0.0)**	**0 (0.0)**	**0 (0.0)**	**0 (0.0)**	**0 (0.0)**	**2 (4.3)**	**0 (0.0)**	**0 (0.0)**	**0 (0.0)**	**2 (4.3)**	**24 (52.2)**	**4 (8.7)**	**4 (8.7)**	**9 (19.6)**	**46 (100)**	**0**	**1**
Patient drug information request	0	0	0	0	0	0	0	0	0	0	0	5 (10.9)	1 (2.2)	0	0	6 (13.0)	0	0
Confusion about therapy	1 (2.2)	0	0	0	0	0	0	0	0	0	0	5 (10.9)	1 (2.2)	0	3 (6.5)	10 (21.7)	0	0
Demonstration of device	0	0	0	0	0	0	2 (4.3)	0	0	0	2 (4.3)	4 (8.7)	0	1 (2.2)	0	9 (19.6)	0	0
Disease management or advice	0	0	0	0	0	0	0	0	0	0	0	9 (19.6)	0	3 (6.5)	5 (10.9)	17 (37.0)	0	0
Other education or information problem	0	0	0	0	0	0	0	0	0	0	0	1 (2.2)	2 (4.3)	0	1 (2.2)	4 (8.7)	0	1
Non-clinical	**1 (1.7)**	**13 (22.0)**	**1 (1.7)**	**0 (0.0)**	**0 (0.0)**	**0 (0.0)**	**4 (6.8)**	**0 (0.0)**	**3 (5.1)**	**2 (3.4)**	**0 (0.0)**	**17 (28.8)**	**0 (0.0)**	**7 (11.9)**	**11 (18.6)**	**59 (100)**	**0**	**2**
Weight management problem	0	2 (3.4)	0	0	0	0	0	0	1 (1.7)	0	0	4 (6.8)	0	4 (6.8)	1 (1.7)	12 (20.3)	0	1
Dietary problem	1 (1.7)	1 (1.7)	0	0	0	0	0	0	1 (1.7)	1 (1.7)	0	8 (13.6)	0	1 (1.7)	1 (1.7)	14 (23.7)	0	0

	Number (% subtype) of recommendations made to resolve DRPs according to DRP subtypes																	
	Drug or dosage modification								Monitoring		Provision of education or information			For follow-up			No recommendation	
DRP type **DRP subtype**	Drug cease	Drug start	Drug switch	Dose decrease	Dose increase	Dose schedule change	Formulation change	Other therapy change	Laboratory monitoring	Non-laboratory monitoring	Compliance assistance	Patient/carer education	Prescriber information	Follow-up by another	Follow-up by prescriber	Total	No recommendation necessary	No recommendation made
Smoking problem	0	9 (15.3)	0	0	0	0	0	0	0	0	0	1 (1.7)	0	0	3 (5.1)	13 (22.0)	0	1
Alcohol problem	0	0	0	0	0	0	0	0	0	1 (1.7)	0	3 (5.1)	0	0	1 (1.7)	5 (8.5)	0	0
Other non-clinical problem	0	1 (1.7)	1 (1.7)	0	0	0	4 (6.8)	0	1 (1.7)	0	0	1 (1.7)	0	2 (3.4)	5 (8.5)	15 (25.4)	0	0
Toxicity or adverse reaction	**57 (15.9)**	**37 (10.3)**	**85 (23.7)**	**58 (16.2)**	**8 (2.2)**	**8 (2.2)**	**4 (1.1)**	**1 (0.3)**	**53 (14.8)**	**9 (2.5)**	**1 (0.3)**	**20 (5.6)**	**1 (0.3)**	**3 (0.8)**	**13 (3.6)**	**358 (100)**	**3**	**50**
Toxicity caused by dose	3 (0.8)	4 (1.1)	3 (0.8)	19 (5.3)	1 (0.3)	1 (0.3)	0	0	5 (1.4)	0	0	1 (0.3)	0	0	0	37 (10.3)	0	1
Toxicity caused by drug interaction	10 (2.8)	1 (0.3)	9 (2.5)	7 (2.0)	1 (0.3)	0	0	0	6 (1.7)	0	0	5 (1.4)	0	1 (0.3)	0	40 (11.2)	0	7
Toxicity evident	44 (12.3)	30 (8.4)	71 (19.8)	32 (8.9)	6 (1.7)	7 (2.0)	4 (1.1)	1 (0.3)	41 (11.5)	9 (2.5)	1 (0.3)	14 (3.9)	1 (0.3)	2 (0.6)	12 (3.4)	275 (76.8)	3	41
Other toxicity/adverse effect problem	0	2 (0.6)	2 (0.6)	0	0	0	0	0	1 (0.3)	0	0	0	0	0	1 (0.3)	6 (1.7)	0	1
Total	**297 (11.4)**	**458 (17.5)**	**272 (10.4)**	**191 (7.3)**	**226 (8.7)**	**72 (2.8)**	**62 (2.4)**	**5 (0.2)**	**470 (18.0)**	**100 (3.8)**	**101 (3.9)**	**163 (6.2)**	**13 (0.5)**	**47 (1.8)**	**133 (5.1)**	**2610 (100)**	**11**	**106**

The most common type of DRPs involved untreated or undertreated indications. Unsurprisingly, the most frequently made recommendations to resolve these DRPs were for additional drugs or increased doses of current therapies. As discussed previously, recommendations for additional monitoring were also common, and a majority of the recommendations for increased monitoring were to resolve DRPs relating to inadequate monitoring. However, *Monitoring* recommendations were also frequently made to manage drug interaction DRPs, and were more commonly made than recommendations to either change or cease interacting drugs. Recommendations to cease drugs were most frequently made to resolve DRPs relating to a lack of therapeutic indication, drug interactions, toxicities and contra-indications.

A comprehensive list of the number of recommendation types made to resolve DRPs according to the causative drug is shown in Table 152 (Appendix XIX). Briefly, examples of frequently made recommendations to commence new medications included antihypertensives in patients with poorly controlled blood pressure, analgesics in patients with poorly controlled pain, aspirin in patients at high risk of cardiovascular events, and calcium and vitamin D supplements in patients with low bone mineral density. DRPs resulting in recommendations to either reduce drug doses or cease medications were most frequently related to renal insufficiency (most commonly metformin), a lack of indication (especially proton pump inhibitors), and contraindications to tricyclic antidepressants and non-steroidal anti-inflammatory drugs.

5.4.6 Uptake of recommendations

5.4.6.1 Overview

An important aspect of the HMR process is that most of the recommendations made by the pharmacists rely on the GP to enact them for changes in therapy to occur. Additionally, patients must also have agreed to the pharmacists' suggested changes. As described in Section 2.3.1, pharmacists participating in the study provided data regarding the outcomes of the recommendations they made in the HMRs where possible. Outcomes data were available for 560 (84.7%) of the HMRs that were submitted for the study. This equated to 1769 (67.8%) of the total number of recommendations made in the HMRs, and 1565 (67.4%) of the DRPs identified. This

data is presented in Table 81, which shows the number of times each type of recommendation was accepted or otherwise by the GP.

TABLE 81 - OUTCOMES OF PHARMACISTS' RECOMMENDATIONS TO RESOLVE OR PREVENT DRPS - GP ACCEPTANCE OF INDIVIDUAL RECOMMENDATIONS

	OUTCOME OF RECOMMENDATION - NUMBER (%) OF RECOMMENDATIONS						
RECOMMENDATION	RECOMMENDATION TOTALLY ACCEPTED	RECOMMENDATION PARTIALLY ACCEPTED	RECOMMENDATION NOT ACCEPTED	NO ACCEPTANCE NECESSARY	DIFFERENT RESOLUTION	UNKNOWN	TOTAL (EACH ROW TOTALS 100%)
Monitoring	**222 (38.9)**	**9 (1.6)**	**65 (11.4)**	**20 (3.5)**	**19 (3.3)**	**235 (41.2)**	**570**
Laboratory monitoring	189 (40.2)	8 (1.7)	52 (11.1)	12 (2.6)	12 (2.6)	197 (41.9)	470
Non-laboratory monitoring	33 (33.0)	1 (1.0)	13 (13.0)	8 (8.0)	7 (7.0)	38 (38.0)	100
Follow-up required	**80 (44.4)**	**11 (6.1)**	**19 (10.6)**	**2 (1.1)**	**7 (3.9)**	**61 (33.9)**	**180**
Follow-up by prescriber	62 (46.6)	6 (4.5)	14 (10.5)	1 (0.8)	6 (4.5)	44 (33.1)	133
Follow-up by another	18 (38.3)	5 (10.6)	5 (10.6)	1 (2.1)	1 (2.1)	17 (36.2)	47
Education provided	**62 (22.4)**	**7 (2.5)**	**7 (2.5)**	**147 (53.1)**	**12 (4.3)**	**42 (15.2)**	**277**
Patient/carer education	10 (6.1)	4 (2.5)	2 (1.2)	125 (76.7)	5 (3.1)	17 (10.4)	163
Prescriber information	5 (38.5)			6 (46.2)		2 (15.4)	13
Compliance assistance	47 (46.5)	3 (3.0)	5 (5.0)	16 (15.8)	7 (6.9)	23 (22.8)	101
Drug or dosage modification	**516 (32.6)**	**112 (7.1)**	**308 (19.5)**	**51 (3.2)**	**93 (5.9)**	**503 (31.8)**	**1583**
Dose increase	91 (40.3)	12 (5.3)	34 (15.0)	12 (5.3)	13 (5.8)	64 (28.3)	226
Dose decrease	63 (33.0)	12 (6.3)	40 (20.9)	6 (3.1)	10 (5.2)	60 (31.4)	191
Drug cease	109 (36.7)	27 (9.1)	58 (19.5)	3 (1.0)	13 (4.4)	87 (29.3)	297
Drug start	124 (27.1)	38 (8.3)	93 (20.3)	13 (2.8)	20 (4.4)	170 (37.1)	458
Formulation change	26 (41.9)	1 (1.6)	12 (19.4)	1 (1.6)	7 (11.3)	15 (24.2)	62
Dose schedule change	23 (31.9)	2 (2.8)	13 (18.1)	6 (8.3)	4 (5.6)	24 (33.3)	72
Drug switch	80 (29.4)	19 (7.0)	56 (20.6)	10 (3.7)	26 (9.6)	81 (29.8)	272
Other therapy change		1 (20.0)	2 (40.0)			2 (40.0)	5
Total	**880 (33.7)**	**139 (5.3)**	**399 (15.3)**	**220 (8.4)**	**131 (5.0)**	**841 (32.2)**	**2610**
Absence of recommendation				**16 (13.7)**	**16 (13.7)**	**85 (72.6)**	**117**
No recommendation necessary				8 (72.7)	1 (9.1)	2 (18.2)	11
No recommendation made				8 (7.5)	15 (14.2)	83 (78.3)	106

Based on the outcomes data provided, approximately half of the recommendations made by the pharmacists were totally accepted (that is, implemented) by the GP (880 recommendations, 49.7%). A further 139 recommendations (7.9%) were partially accepted, and 220 recommendations (12.4%) required no action by the GP for them to be implemented. This may be interpreted as meaning that about 70% of the pharmacists' recommendations were at least partially implemented in the patients' medication management.

Importantly, in a HMR it is not necessary for a pharmacist's recommendation/s to be accepted by a GP for a DRP to be resolved or managed. In many cases, the pharmacist may make a recommendation to resolve a DRP, but the GP institutes an alternative course of action to address the same DRP. To clarify whether or not the recommendations would have addressed the DRPs that were identified by the pharmacists, further analysis of the outcomes data was performed. The outcomes data were grouped into two categories according to whether or not any action was taken by the GP to resolve the DRPs identified. DRPs with the only outcome classified as "*Not accepted*" were considered to be "*unresolved*"; any DRP that resulted in some resolving action was considered to be "*potentially resolved*". DRPs not requiring any action from the GP (such as educational interventions directed at patients) were also classed as "*potentially resolved*".

The results of this analysis are presented in Table 82. These data imply that over 80% of the DRPs identified in the HMRs potentially would have been addressed in some way. A χ^2 test comparing the proportions of DRP types that were potentially resolved and unresolved identified significant differences between the DRP types (Pearson χ^2=41.53, df=7, P<0.001). The differences appeared to result primarily from a higher rate of potential resolution of *Education and information* and *Compliance and concordance* DRPs compared to *Drug selection* and *Dose* DRPs. It is also noteworthy that DRPs relating to too-high doses and medications without indications had relatively low rates of potential resolution compared to the remaining DRP types.

The value of 81.8% (the proportion of all *potentially resolved* DRPs) was used for the baseline scenario in the economic analysis as an estimate of the uptake of the pharmacists' recommendations for HMRs that did not have outcomes data (see

Chapter 6). The value was modified in the scenario analysis to examine the sensitivity of the model to its effects (Section 6.4).

TABLE 82 - POTENTIAL RESOLUTION OF DRPS ACCORDING TO DRP SUBTYPE

DRP SUBTYPE	POTENTIALLY RESOLVED	UNRESOLVED	TOTAL
Drug selection	**266 (17.0)**	**81 (5.2)**	**347 (22.2)**
Duplication	27 (1.7)	3 (0.2)	30 (1.9%)
Drug interaction	91 (5.8)	23 (1.5)	114 (7.3%)
Wrong drug	1 (0.1)	0 (0.0)	1 (0.1%)
Wrong dosage form	1 (0.1)	1 (0.1)	2 (0.1%)
Unnecessary therapy/no apparent current indication	59 (3.8)	25 (1.6)	84 (5.4%)
Contraindications apparent	81 (5.2)	26 (1.7)	107 (6.8%)
Other drug selection problem	6 (0.4)	3 (0.2)	9 (0.6%)
Over or underdose prescribed	**104 (6.6)**	**36 (2.3)**	**140 (8.9)**
Dose too high	60 (3.8)	26 (1.7)	86 (5.5%)
Dose too low	27 (1.7)	3 (0.2)	30 (1.9%)
Other dose problem	17 (1.1)	7 (0.4)	24 (1.5%)
Compliance & concordance	**232 (14.8)**	**18 (1.2)**	**250 (16.0)**
Taking too little	99 (6.3)	5 (0.3)	104 (6.6%)
Taking too much	10 (0.6)	0 (0.0)	10 (0.6%)
Difficulty using dosage form	31 (2.0)	4 (0.3)	35 (2.2%)
Patient using out of date medication	13 (0.8)	1 (0.1)	14 (0.9%)
Other compliance problem	79 (5.0)	8 (0.5)	87 (5.6%)
Untreated indications	**332 (21.2)**	**87 (5.6)**	**419 (26.8)**
Condition not adequately treated	204 (13.0)	47 (3.0)	251 (16.0%)
Therapy required	127 (8.1)	40 (2.6)	167 (10.7%)
Other untreated indication problem	1 (0.1)	0 (0.0)	1 (0.1%)
Monitoring	**122 (7.8)**	**21 (1.3)**	**143 (9.1)**
Laboratory monitoring	108 (6.9)	19 (1.2)	127 (8.1%)
Non-laboratory monitoring	11 (0.7)	2 (0.1)	13 (0.8%)
Other monitoring problem	3 (0.2)	0 (0.0)	3 (0.2%)
Education or information	**34 (2.2)**	**2 (0.1)**	**36 (2.3)**
Patient drug information request	6 (0.4)	0 (0.0)	6 (0.4%)
Confusion about therapy	6 (0.4)	1 (0.1)	7 (0.4%)
Demonstration of device	8 (0.5)	0 (0.0)	8 (0.5%)
Disease management or advice	10 (0.6)	1 (0.1)	11 (0.7%)
Other education or information problem	4 (0.3)	0 (0.0)	4 (0.3%)
Non-clinical	**35 (2.2)**	**3 (0.2)**	**38 (2.4)**
Weight management problem	7 (0.4)	1 (0.1)	8 (0.5%)
Dietary problem	11 (0.7)	0 (0.0)	11 (0.7%)
Smoking problem	7 (0.4)	1 (0.1)	8 (0.5%)
Alcohol problem	1 (0.1)	0 (0.0)	1 (0.1%)
Other non-clinical problem	9 (0.6)	1 (0.1)	10 (0.6%)
Toxicity or adverse reaction	**155 (9.9)**	**37 (2.4)**	**192 (12.3)**
Toxicity caused by dose	13 (0.8)	4 (0.3)	17 (1.1%)
Toxicity caused by drug interaction	20 (1.3)	4 (0.3)	24 (1.5%)

DRP SUBTYPE	POTENTIALLY RESOLVED	UNRESOLVED	TOTAL
Toxicity evident	119 (7.6)	29 (1.9)	148 (9.5%)
Other toxicity/adverse effect problem	3 (0.2)	0 (0.0)	3 (0.2%)
Total	**1280 (81.8)**	**285 (18.2)**	**1565 (100.0)**

For DRP types, Pearson χ^2=41.53, df=7, *P*<0.001

5.4.6.2 Resolution of DRPs involving drugs of specific interest

Many of the drugs of specific interest discussed in Section 5.4.3.2 have been associated with adverse events in numerous studies of patient groups such as those in this study. Further investigation of the interventions involving these drugs by assessment of the rates of DRP resolution for each drug or drug class was undertaken to provide some indication as to whether the HMRs may have affected the management of the patients taking these drugs.

5.4.6.2.1 Warfarin

The proportions of the DRPs involving warfarin in patients taking it that were potentially resolved and unresolved are shown in Table 83. Aside from *Drug interaction* and *Toxicity DRPs*, the data is of reasonably low numbers and it is difficult to draw conclusions from it. In general, a majority of the DRPs were addressed in some way, which may be interpreted as meaning the HMR were likely to have improved the management of these patients' warfarin therapy.

TABLE 83 - PROPORTION OF RESOLVED AND UNRESOLVED DRPS INVOLVING WARFARIN IN PATIENTS TAKING IT

DRP TYPE	DRP SUBTYPE	NUMBER (%) OF DRPS			
		Resolved *	Not resolved *	Total **	Unknown **
Drug selection	Duplication	1 (2.3)	1 (2.3)	**2 (3.2)**	
	Drug interaction	12 (27.3)	4 (9.1)	**26 (41.3)**	10 (15.9)
	Unnecessary therapy/no apparent current indication		1 (2.3)	**4 (6.3)**	3 (4.8)
	Contraindications apparent	1 (2.3)	1 (2.3)	**2 (3.2)**	
Over or underdose prescribed	Dose too high		1 (2.3)	**1 (1.6)**	
	Other Dose Problem	1 (2.3)		**1 (1.6)**	
Compliance	Taking too little	1 (2.3)		**1 (1.6)**	
	Other Compliance Problem	1 (2.3)	2 (4.5)	**3 (4.8)**	
Untreated indications	Condition not adequately treated		1 (2.3)	**1 (1.6)**	
	Therapy required			**2 (3.2)**	2 (3.2)
Monitoring	Laboratory Monitoring	2 (4.5)		**4 (6.3)**	2 (3.2)
Education or Information	Patient drug information request	2 (4.5)		**2 (3.2)**	
Non-clinical	Dietary problem	2 (4.5)		**2 (3.2)**	
	Other non-clinical problem	1 (2.3)		**1 (1.6)**	
Toxicity or Adverse reaction	Toxicity caused by dose	1 (2.3)		**1 (1.6)**	
	Toxicity caused by drug interaction	4 (9.1)		**5 (7.9)**	1 (1.6)
	Toxicity evident	3 (6.8)	1 (2.3)	**5 (7.9)**	1 (1.6)
Total		**32 (72.7)**	**12 (27.3)**	**63 (100)**	**19 (30.2)**

* percentage of warfarin-related DRP subtypes with outcomes known
** percentage of total number of warfarin-related DRPs (outcomes both known and unknown)

5.4.6.2.2 Digoxin

Similarly, there was limited data available regarding the management of the DRPs involving digoxin (Table 84). In contrast to the warfarin-related DRPs where approximately 70% were addressed, over 90% of the digoxin-related DRPs were resolved or managed following the HMR. This may have resulted from a greater proportion of recommendations made for increased therapeutic monitoring for the digoxin DRPs compared to those involving warfarin (62% versus 34%, Table 83).

TABLE 84 - PROPORTION OF RESOLVED AND UNRESOLVED DRPS INVOLVING DIGOXIN IN PATIENTS TAKING IT

DRP TYPE	DRP SUBTYPE	NUMBER (%) OF DRPS			
		Resolved *	Not resolved *	Total **	Unknown **
Drug selection	Duplication	1 (2.4)		**1 (1.9)**	
	Drug interaction	10 (24.4)	1 (2.4)	**14 (26.4)**	3 (5.7)
Over or underdose prescribed	Dose too high	4 (9.8)		**4 (7.5)**	
	Dose too low	1 (2.4)		**1 (1.9)**	
	Other Dose Problem	2 (4.9)		**2 (3.8)**	
Compliance	Taking too little	2 (4.9)		**2 (3.8)**	
Untreated indications	Condition not adequately treated			**2 (3.8)**	2 (3.8)
Monitoring	Laboratory Monitoring	6 (14.6)	2 (4.9)	**13 (24.5)**	5 (9.4)
	Other Monitoring Problem	1 (2.4)		**1 (1.9)**	
Toxicity or Adverse reaction	Toxicity caused by dose	2 (4.9)		**2 (3.8)**	
	Toxicity caused by drug interaction	3 (7.3)	1 (2.4)	**4 (7.5)**	
	Toxicity evident	5 (12.2)		**7 (13.2)**	2 (3.8)
Total		**37 (90.2)**	**4 (9.8)**	**53 (100)**	**12 (22.6)**

* percentage of digoxin-related DRP subtypes with outcomes known
** percentage of total number of digoxin-related DRPs (outcomes both known and unknown)

5.4.6.2.3 Proton pump inhibitors

The proportions of potentially resolved and unresolved DRPs involving proton pump inhibitors in patients taking them are shown in Table 85. Whilst the numbers of unresolved DRPs are low, it is notable that there seems to be a greater proportion of unresolved DRPs involving too-high doses and unnecessary therapy than the remaining DRP subtypes, particularly those relating to laboratory monitoring.

TABLE 85 - PROPORTION OF RESOLVED AND UNRESOLVED DRPS INVOLVING PROTON PUMP INHIBITORS IN PATIENTS TAKING THEM

DRP TYPE	DRP SUBTYPE	NUMBER (%) OF DRPS			
		Resolved *	Not resolved *	Total **	Unknown **
Drug selection	Duplication	3 (2.8)		**3 (1.8)**	
	Drug interaction	2 (1.9)	1 (0.9)	**7 (4.3)**	4 (2.4)
	Unnecessary therapy/no apparent current indication	12 (11.3)	5 (4.7)	**30 (18.3)**	13 (7.9)
	Contraindications apparent	3 (2.8)		**4 (2.4)**	1 (0.6)
Over or underdose prescribed	Dose too high	11 (10.4)	5 (4.7)	**23 (14.0)**	7 (4.3)
	Dose too low	1 (0.9)		**1 (0.6)**	
	Other Dose Problem			**1 (0.6)**	1 (0.6)
Compliance	Taking too little	2 (1.9)	1 (0.9)	**3 (1.8)**	
	Taking too much	2 (1.9)		**2 (1.2)**	
	Difficulty using dosage form	2 (1.9)	2 (1.9)	**4 (2.4)**	
	Other Compliance Problem	3 (2.8)		**3 (1.8)**	
Untreated indications	Condition not adequately treated	7 (6.6)	2 (1.9)	**13 (7.9)**	4 (2.4)
	Therapy required	1 (0.9)	1 (0.9)	**2 (1.2)**	
Monitoring	Laboratory Monitoring	19 (17.9)	1 (0.9)	**38 (23.2)**	18 (11.0)
Toxicity or Adverse reaction	Toxicity caused by dose	1 (0.9)		**1 (0.6)**	
	Toxicity caused by drug interaction	1 (0.9)		**4 (2.4)**	3 (1.8)
	Toxicity evident	12 (11.3)	4 (3.8)	**23 (14.0)**	7 (4.3)
	Other Toxicity/Adverse Effect problem	2 (1.9)		**2 (1.2)**	
Total		**84 (79.2)**	**22 (20.8)**	**164 (100)**	**58 (35.4)**

* percentage of proton pump inhibitor-related DRP subtypes with outcomes known
** percentage of total number of proton pump inhibitor-related DRPs (outcomes both known and unknown)

5.4.6.2.4 Paracetamol

The resolution frequency of the DRPs involving paracetamol is shown in Table 86. It is unsurprising that there was a high proportion of potentially resolved DRPs involving paracetamol as it is not a prescription-only drug and the pharmacists may have resolved the DRPs without needing to involve the GP in many cases.

TABLE 86 - PROPORTION OF RESOLVED AND UNRESOLVED DRPS INVOLVING PARACETAMOL IN PATIENTS TAKING IT

DRP TYPE	DRP SUBTYPE	NUMBER (%) OF DRPS			
		Resolved *	Not resolved *	Total **	Unknown **
Drug selection	Drug interaction	5 (5.6)		**8 (6.3)**	3 (2.4)
	Contraindications apparent	1 (1.1)	1 (1.1)	**3 (2.4)**	1 (0.8)
Over or underdose prescribed	Dose too high	2 (2.2)		**3 (2.4)**	1 (0.8)
	Dose too low	1 (1.1)		**1 (0.8)**	
	Other Dose Problem	1 (1.1)		**1 (0.8)**	
Compliance	Taking too little	3 (3.4)		**3 (2.4)**	
	Taking too much	1 (1.1)		**1 (0.8)**	
	Difficulty using dosage form	1 (1.1)		**2 (1.6)**	1 (0.8)
	Other Compliance Problem	1 (1.1)		**3 (2.4)**	2 (1.6)
Untreated indications	Condition not adequately treated	54 (60.7)	11 (12.4)	**93 (73.8)**	28 (22.2)
	Therapy required			**1 (0.8)**	1 (0.8)
Monitoring	Laboratory Monitoring	2 (2.2)		**2 (1.6)**	
Non-clinical	Other non-clinical problem	1 (1.1)		**1 (0.8)**	
Toxicity or Adverse reaction	Toxicity caused by dose	1 (1.1)		**1 (0.8)**	
	Toxicity caused by drug interaction	2 (2.2)		**2 (1.6)**	
	Toxicity evident	1 (1.1)		**1 (0.8)**	
Total		**77 (86.5)**	**12 (13.5)**	**126 (100)**	**37 (29.4)**

* percentage of paracetamol-related DRP subtypes with outcomes known
** percentage of total number of paracetamol-related DRPs (outcomes both known and unknown)

5.4.6.2.5 HMG-CoA reductase inhibitors

In contrast to the DRPs involving paracetamol, the DRPs related to therapy with HMG-CoA reductase inhibitors were less frequently resolved or managed (Table 87). For the DRPs involving these drugs, only two out of every three DRPs of the most commonly occurring DRP subtypes (*Drug interaction*, *Condition not adequately treated* and *Toxicity evident*) were resolved or managed as a result of the HMR. It is somewhat concerning that this was despite the pharmacist identifying the presence of an actual ADR in the *Toxicity* DRPs. It is possible that the GPs often considered that the signs or symptoms that the pharmacists attributed to these drugs were of a different aetiology and not caused by the patients' HMG-CoA reductase inhibitor therapy.

TABLE 87 - PROPORTION OF RESOLVED AND UNRESOLVED DRPS INVOLVING HMG-COA REDUCTASE INHIBITORS IN PATIENTS TAKING THEM

DRP TYPE	DRP SUBTYPE	NUMBER (%) OF DRPS			
		Resolved *	Not resolved *	Total **	Unknown **
Drug selection	Duplication	1 (1.3)		**2 (1.6)**	1 (0.8)
	Drug interaction	15 (18.8)	5 (6.3)	**26 (21.1)**	6 (4.9)
	Unnecessary therapy/no apparent current indication	1 (1.3)	1 (1.3)	**3 (2.4)**	1 (0.8)
Over or underdose prescribed	Dose too high	2 (2.5)	1 (1.3)	**7 (5.7)**	4 (3.3)
	Dose too low		1 (1.3)	**1 (0.8)**	
	Other Dose Problem	1 (1.3)	1 (1.3)	**3 (2.4)**	1 (0.8)
Compliance	Taking too little	3 (3.8)		**4 (3.3)**	1 (0.8)
	Difficulty using dosage form	2 (2.5)		**2 (1.6)**	
	Other Compliance Problem	1 (1.3)	1 (1.3)	**3 (2.4)**	1 (0.8)
Untreated indications	Condition not adequately treated	11 (13.8)	5 (6.3)	**22 (17.9)**	6 (4.9)
Monitoring	Laboratory Monitoring	9 (11.3)	2 (2.5)	**20 (16.3)**	9 (7.3)
Education or Information	Other Education or Information Problem	1 (1.3)		**1 (0.8)**	
Non-clinical	Other non-clinical problem			**1 (0.8)**	1 (0.8)
Toxicity or Adverse reaction	Toxicity caused by dose			**2 (1.6)**	2 (1.6)
	Toxicity caused by drug interaction	1 (1.3)		**2 (1.6)**	1 (0.8)
	Toxicity evident	10 (12.5)	5 (6.3)	**24 (19.5)**	9 (7.3)
Total		**58 (72.5)**	**22 (27.5)**	**123 (100)**	**43 (35.0)**

* percentage of HMG-CoA reductase inhibitor-related DRP subtypes with outcomes known
** percentage of total number of HMG-CoA reductase inhibitor-related DRPs (outcomes both known and unknown)

5.4.6.2.6 Antiplatelet agents

There were some similarities between the frequency of resolution of the common DRPs involving antiplatelet drugs and HMG-CoA reductase inhibitors (Table 88). There was an approximately equivalent frequency of unresolved ADR DRPs related to antiplatelet drugs, and an even greater proportion of unresolved drug interaction DRPs than in those involving HMG-CoA reductase inhibitors. Consequently, the overall frequency of DRP resolution was low compared to the resolution of DRP types (65.7% versus 81.8%).

TABLE 88 - PROPORTION OF RESOLVED AND UNRESOLVED DRPS INVOLVING ANTIPLATELET AGENTS IN PATIENTS TAKING THEM

DRP TYPE	DRP SUBTYPE	NUMBER (%) OF DRPS			
		Resolved *	Not resolved *	Total **	Unknown **
Drug selection	Duplication	5 (7.5)	3 (4.5)	**9 (8.7)**	1 (1.0)
	Drug interaction	11 (16.4)	10 (14.9)	**35 (34.0)**	14 (13.6)
	Unnecessary therapy/no apparent current indication	2 (3.0)	2 (3.0)	**7 (6.8)**	3 (2.9)
	Contraindications apparent		1 (1.5)	**1 (1.0)**	
Over or underdose prescribed	Dose too high	1 (1.5)		**2 (1.9)**	1 (1.0)
Compliance	Taking too little	8 (11.9)		**9 (8.7)**	1 (1.0)
	Taking too much	1 (1.5)		**1 (1.0)**	
	Other Compliance Problem			**1 (1.0)**	1 (1.0)
Untreated indications	Condition not adequately treated	2 (3.0)		**2 (1.9)**	
	Therapy required	1 (1.5)	2 (3.0)	**4 (3.9)**	1 (1.0)
Monitoring	Laboratory Monitoring			**1 (1.0)**	1 (1.0)
Non-clinical	Alcohol problem			**2 (1.9)**	2 (1.9)
	Other non-clinical problem	2 (3.0)		**2 (1.9)**	
Toxicity or Adverse reaction	Toxicity caused by drug interaction	2 (3.0)	1 (1.5)	**7 (6.8)**	4 (3.9)
	Toxicity evident	9 (13.4)	4 (6.0)	**19 (18.4)**	6 (5.8)
	Other Toxicity/Adverse Effect problem			**1 (1.0)**	1 (1.0)
Total		**44 (65.7)**	**23 (34.3)**	**103 (100)**	**36 (35.0)**

* percentage of antiplatelet-related DRP subtypes with outcomes known
** percentage of total number of antiplatelet-related DRPs (outcomes both known and unknown)

5.4.6.2.7 ACE inhibitors and angiotensin 2 receptor antagonists

The proportions of potentially resolved and unresolved DRPs involving ACE inhibitors and angiotensin 2 receptor antagonists in patients taking them are shown in Table 89. Despite the proportion of potentially resolved DRPs being greater than those seen with HMG-CoA reductase inhibitors and antiplatelet agents, a similarly low proportion of resolved *Toxicity* DRPs was again noted. This was offset by a high frequency of resolution of *Drug interaction* DRPs, resulting in the overall frequency of DRP resolution for this drug group being aligned with the overall sample of DRPs.

TABLE 89 - PROPORTION OF RESOLVED AND UNRESOLVED DRPS INVOLVING ACE INHIBITORS AND ANGIOTENSIN 2 RECEPTOR ANTAGONISTS IN PATIENTS TAKING THEM

DRP TYPE	DRP SUBTYPE	NUMBER (%) OF DRPS			
		Resolved *	Not resolved *	Total **	Unknown **
Drug selection	Duplication			**1 (0.5)**	1 (0.5)
	Drug interaction	34 (28.3)	4 (3.3)	**55 (27.6)**	17 (8.5)
	Unnecessary therapy/no apparent current indication	2 (1.7)		**3 (1.5)**	1 (0.5)
	Contraindications apparent	2 (1.7)	2 (1.7)	**4 (2.0)**	
	Other drug selection problem	1 (0.8)		**2 (1.0)**	1 (0.5)
Over or underdose prescribed	Dose too high	3 (2.5)	2 (1.7)	**6 (3.0)**	1 (0.5)
	Dose too low	4 (3.3)	1 (0.8)	**7 (3.5)**	2 (1.0)
Compliance	Taking too little	2 (1.7)		**2 (1.0)**	
	Other Compliance Problem	2 (1.7)	1 (0.8)	**5 (2.5)**	2 (1.0)
Untreated indications	Condition not adequately treated	14 (11.7)	3 (2.5)	**36 (18.1)**	19 (9.5)
	Therapy required	1 (0.8)	1 (0.8)	**3 (1.5)**	1 (0.5)
Monitoring	Laboratory Monitoring	12 (10.0)	3 (2.5)	**28 (14.1)**	13 (6.5)
	Non-Laboratory monitoring	3 (2.5)		**3 (1.5)**	
Education or Information	Other Education or Information Problem	1 (0.8)		**1 (0.5)**	
Non-clinical	Dietary problem	1 (0.8)		**1 (0.5)**	
Toxicity or Adverse reaction	Toxicity caused by dose	2 (1.7)		**2 (1.0)**	
	Toxicity caused by drug interaction	3 (2.5)		**5 (2.5)**	2 (1.0)
	Toxicity evident	12 (10.0)	4 (3.3)	**35 (17.6)**	19 (9.5)
Total		**99 (82.5)**	**21 (17.5)**	**199 (100)**	**79 (39.7)**

* percentage of ACE inhibitor and angiotensin 2 receptor antagonist -related DRP subtypes with outcomes known
** percentage of total number of ACE inhibitor and angiotensin 2 receptor antagonist -related DRPs (outcomes both known and unknown)

5.4.6.2.8 Non-steroidal anti-inflammatory drugs

Table 90 shows the proportions of DRPs involving non-steroidal anti-inflammatory drugs that were potentially resolved and unresolved following the HMR. The proportion of NSAID-related DRPs that were potentially resolved was slightly higher than the overall proportion of potentially resolved DRPs, perhaps indicative of a high level of GP concern regarding these drugs in the patient group, especially with regards to drug interactions.

TABLE 90 - PROPORTION OF RESOLVED AND UNRESOLVED DRPS INVOLVING NON-STEROIDAL ANTI-INFLAMMATORY DRUGS IN PATIENTS TAKING THEM

DRP TYPE	DRP SUBTYPE	NUMBER (%) OF DRPS			
		Resolved *	Not resolved *	Total **	Unknown **
Drug selection	Duplication	3 (3.3)		**3 (2.6)**	
	Drug interaction	27 (29.7)	2 (2.2)	**40 (34.5)**	11 (9.5)
	Unnecessary therapy/no apparent current indication	1 (1.1)		**3 (2.6)**	2 (1.7)
	Contraindications apparent	17 (18.7)	6 (6.6)	**25 (21.6)**	2 (1.7)
Over or underdose prescribed	Dose too high	4 (4.4)	1 (1.1)	**5 (4.3)**	
	Dose too low	3 (3.3)		**4 (3.4)**	1 (0.9)
Compliance	Taking too little	1 (1.1)		**1 (0.9)**	
	Other Compliance Problem	1 (1.1)		**1 (0.9)**	
Untreated indications	Condition not adequately treated	10 (11.0)	2 (2.2)	**16 (13.8)**	4 (3.4)
Monitoring	Laboratory Monitoring		1 (1.1)	**1 (0.9)**	
Education or Information	Confusion about therapy	1 (1.1)		**1 (0.9)**	
	Other Education or Information Problem	1 (1.1)		**1 (0.9)**	
Toxicity or Adverse reaction	Toxicity caused by drug interaction	2 (2.2)		**2 (1.7)**	
	Toxicity evident	6 (6.6)	1 (1.1)	**12 (10.3)**	5 (4.3)
	Other Toxicity/Adverse Effect problem	1 (1.1)		**1 (0.9)**	
Total		**78 (85.7)**	**13 (14.3)**	**116 (100)**	**25 (21.6)**

* percentage of non-steroidal anti-inflammatory drug-related DRP subtypes with outcomes known
** percentage of total number of non-steroidal anti-inflammatory drug-related DRPs (outcomes both known and unknown)

5.4.6.2.9 Diuretics

A similarly high frequency of potential DRP resolution was observed with the DRPs involving diuretic usage (Table 91). This may have partially resulted from a substantial number of DRPs involving drug interactions between diuretics and NSAIDs, as the frequency of resolution of this subtype of DRPs is similar to that observed in Table 90.

TABLE 91 - PROPORTION OF RESOLVED AND UNRESOLVED DRPS INVOLVING DIURETICS IN PATIENTS TAKING THEM

DRP TYPE	DRP SUBTYPE	NUMBER (%) OF DRPS			
		Resolved *	Not resolved *	Total **	Unknown **
Drug selection	Duplication	1 (1.5)		**2 (1.8)**	1 (0.9)
	Drug interaction	23 (33.8)	3 (4.4)	**33 (29.2)**	7 (6.2)
	Unnecessary therapy/no apparent current indication	3 (4.4)	2 (2.9)	**8 (7.1)**	3 (2.7)
	Contraindications apparent	1 (1.5)	1 (1.5)	**2 (1.8)**	
Over or underdose prescribed	Dose too high	1 (1.5)	1 (1.5)	**6 (5.3)**	4 (3.5)
	Dose too low			**1 (0.9)**	1 (0.9)
	Other Dose Problem	1 (1.5)		**1 (0.9)**	
Compliance	Taking too little	2 (2.9)		**5 (4.4)**	3 (2.7)
	Other Compliance Problem	1 (1.5)		**3 (2.7)**	2 (1.8)
Untreated indications	Condition not adequately treated	3 (4.4)	2 (2.9)	**7 (6.2)**	2 (1.8)
	Therapy required	2 (2.9)	1 (1.5)	**3 (2.7)**	
Monitoring	Laboratory Monitoring	7 (10.3)		**13 (11.5)**	6 (5.3)
Toxicity or Adverse reaction	Toxicity caused by dose			**4 (3.5)**	4 (3.5)
	Toxicity caused by drug interaction	4 (5.9)	1 (1.5)	**8 (7.1)**	3 (2.7)
	Toxicity evident	8 (11.8)		**17 (15.0)**	9 (8.0)
Total		**57 (83.8)**	**11 (16.2)**	**113 (100)**	**45 (39.8)**

* percentage of diuretic-related DRP subtypes with outcomes known
** percentage of total number of diuretic-related DRPs (outcomes both known and unknown)

5.5 Summary of results

In summary, the major findings of this facet of the VALMER study were as follows:

- One hundred and forty nine pharmacists submitted six hundred and sixty-one HMRs for analysis in the study. The general demographics of the patients who received HMRs were consistent with those reported in previous research of HMRs.
- The HMR reports documented 2323 DRPs, of which the most common were *Condition not adequately treated* (16.5% of DRPs), *Therapy required* (11.3%) and *Toxicity evident* (10.6%).
- Comparatively few DRPs relating to patient *Education or information* were documented; however it is likely that substantially more education and counselling was provided during the HMR interview.

- The most common DRP was inadequate pain management which was identified in 118 (17.9%) patients.
- Drug groups commonly involved in DRPs were anti-thrombotics, acid-suppressing therapies, and lipid modifying agents.
- The pharmacists made 2727 recommendations to resolve the DRPs. The most frequently made recommendations included performing laboratory monitoring, commencing new medications (particularly analgesics and cardiovascular drugs), or ceasing others (such as acid-suppressing drugs).
- Information relating to the outcomes of the recommendations made to resolve the DRPs was available for 66% of the data (1801 recommendations). Of these recommendations, 1565 (87%) required the prescriber to implement them. Approximately 80% of the DRPs were addressed in some way.

The estimated clinical and economic outcomes of the HMRs are presented in the following chapter.

Chapter 6 - Results of the VALMER study: potential clinical and economic outcomes of HMRs

6.1 Introduction

The results of the clinical and economic evaluation of the HMRs are presented in this chapter. The chapter commences with an analysis of the potential changes in drug costs that occurred following the HMRs. The results of the impacts on quality of life and health resource utilisation as a consequence of the HMRs, as estimated by the expert panel, are then examined in detail.

6.2 Drug cost analysis

The perspective of the cost analysis was from that of the Australian government, so only PBS-listed items were included in the drug cost analysis. In calculating the changes in drug costs resulting from the HMRs, it was assumed that any changes to the patients' medication regimens would be sustained for 12 months following the HMR. Documentation regarding the frequency of medications taken on a when-required basis was poor in most of the HMR reports. To minimise errors in the measurement of the cost of these drugs, they were excluded from the analysis.

Prior to excluding these drugs from the analysis, a sensitivity analysis involving several estimates of the costs of these drugs was considered. However, it was concluded from an initial investigation of the recommendations involving these drugs that excluding them from the drug cost analysis was unlikely to adversely affect the validity of the results. This was because a majority of the drugs taken on a when-required basis were of comparatively minor cost to the PBS, such as paracetamol ($6.99 for 180 tablets), temazepam ($2.46 for 25 tablets) and salbutamol ($9.79 for 400 puffs).[210] It was considered that proportional changes to the frequency of use of these drugs would result in substantially smaller changes in costs than those resulting from changes to regular medications. Furthermore, fewer than 7% of the recommendations involved these drugs. Consequently, the proposed sensitivity analysis was considered unnecessary.

6.2.1 Drug costs before HMR

Of the 6346 drugs taken by the patients on a regular basis at the time of the HMR, 4891 (77%) were subsidised by the PBS. The median total monthly cost per patient of these drugs was $198.96 (IQR $154.48). At the baseline assumption of a patient contribution of $5 per item, the median monthly cost to the PBS was $165.88 (IQR $140.85) per patient per month. As shown in Figure 39, there was substantial variation between patients with regards to the monthly drug cost to the PBS.

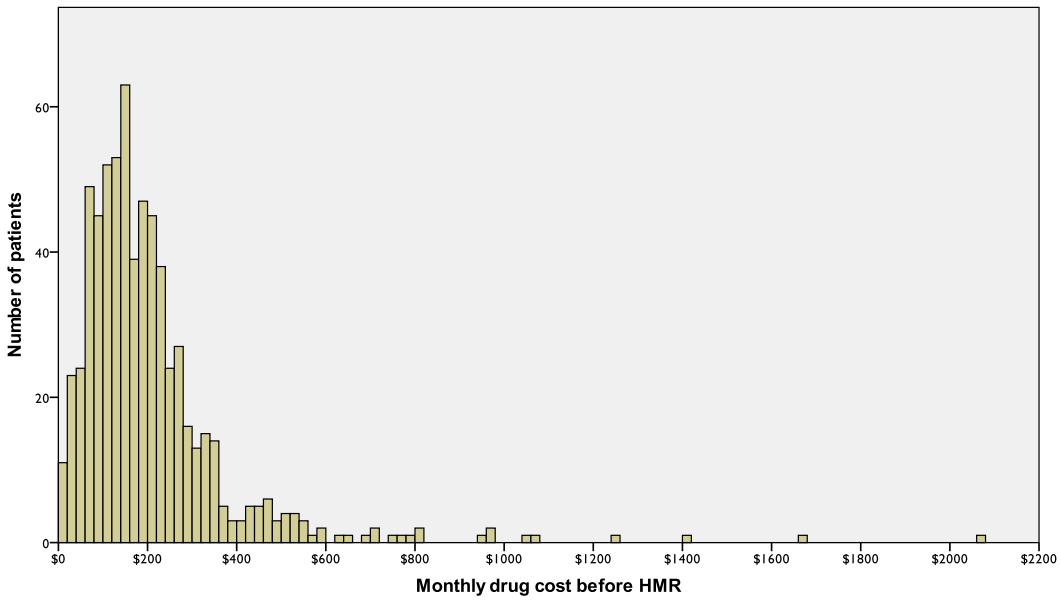

FIGURE 39 - DISTRIBUTION OF MONTHLY DRUG COSTS TO THE PBS PER PATIENT PRIOR TO THE HMR

The contribution of each group of medication classified according to ATC level one and two categories to the monthly PBS drug cost is shown in Table 92. Cardiovascular medications accounted for the greatest proportion of the total monthly PBS drug cost, which was consistent with the high prevalence of cardiovascular disease in the patient cohort. This group of drugs accounted for approximately twice the cost per month as the next most costly drug group, drugs for alimentary tract and metabolism disorders.

TABLE 92 - MONTHLY DRUG COST OF PBS-SUBSIDISED ITEMS TAKEN ON A REGULAR BASIS AT TIME OF HMR (DOES NOT INCLUDE WHEN-REQUIRED OR NON-PBS MEDICATIONS)

DRUG CLASS (ATC LEVEL 1) ATC LEVEL 2	NUMBER (% OF TOTAL)		AVERAGE MONTHLY DRUG COST PER PATIENT ($)	
	PATIENTS TAKING	ITEMS	TOTAL	TO PBS*
Alimentary tract and metabolism	**478 (72.3)**	**788 (16.1)**	**42.28**	**37.05**
Antidiarrhoeals, intestinal anti-inflammatory/antiinfectives	19 (2.9)	19 (0.4)	1.46	1.32
Antiobesity preparations, excl. diet products	1 (0.2)	1 (0.0)	0.19	0.19
Digestives, incl. enzymes	1 (0.2)	1 (0.0)	0.13	0.13
Drugs for acid related disorders	330 (49.9)	338 (6.9)	20.58	17.78
Drugs for functional gastrointestinal disorders	14 (2.1)	20 (0.4)	0.61	0.38
Drugs used in diabetes	196 (29.7)	321 (6.6)	18.12	16.41
Laxatives	21 (3.2)	22 (0.4)	0.57	0.39
Mineral supplements	56 (8.5)	56 (1.1)	0.34	0.21
Vitamins	10 (1.5)	10 (0.2)	0.29	0.25
Anti-infectives for systemic use	**26 (3.9)**	**28 (0.6)**	**1.44**	**1.10**
Antibacterials for systemic use	25 (3.8)	26 (0.5)	0.79	0.46
Antimycotics for systemic use	1 (0.2)	1 (0.0)	0.42	0.41
Antivirals for systemic use	1 (0.2)	1 (0.0)	0.23	0.23
Antineoplastic and immunomodulating agents	**37 (5.6)**	**60 (1.2)**	**10.73**	**10.35**
Antineoplastic agents	18 (2.7)	18 (0.4)	0.43	0.31
Endocrine therapy	13 (2.0)	14 (0.3)	3.53	3.47
Immunosuppressive agents	25 (3.8)	28 (0.6)	6.77	6.57
Antiparasitic products, insecticides and repellents	**6 (0.9)**	**6 (0.1)**	**0.17**	**0.15**
Antiprotozoals	6 (0.9)	6 (0.1)	0.17	0.15
Blood and blood forming organs	**473 (71.6)**	**597 (12.2)**	**25.27**	**21.92**
Anti-anaemic preparations	82 (12.4)	86 (1.8)	6.84	6.56
Antihaemorrhagics	1 (0.2)	1 (0.0)	0.08	0.07
Antithrombotic agents	450 (68.1)	510 (10.4)	18.35	15.29
Cardiovascular system	**628 (95.0)**	**1910 (39.1)**	**76.44**	**64.26**
Agents acting on the renin-angiotensin system	452 (68.4)	492 (10.1)	17.62	13.79
Antihypertensives	50 (7.6)	54 (1.1)	0.78	0.54
Beta blocking agents	234 (35.4)	238 (4.9)	5.66	4.24
Calcium channel blockers	195 (29.5)	200 (4.1)	5.90	4.44
Cardiac therapy	178 (26.9)	212 (4.3)	4.48	3.40
Diuretics	205 (31.0)	265 (5.4)	1.71	0.95
Serum lipid reducing agents	428 (64.8)	449 (9.2)	40.29	36.90
Dermatologicals	**7 (1.1)**	**8 (0.2)**	**0.62**	**0.58**
Antifungals for dermatological use	1 (0.2)	2 (0.0)	0.22	0.21
Antipsoriatics	4 (0.6)	4 (0.1)	0.35	0.33
Corticosteroids, dermatological preparations	2 (0.3)	2 (0.0)	0.05	0.03

Drug class (ATC level 1) ATC level 2	Number (% of total)		Average monthly drug cost per patient ($)	
	Patients taking	Items	Total	To PBS*
Genitourinary system and sex hormones	**45 (6.8)**	**56 (1.1)**	**2.88**	**2.59**
Sex hormones and modulators of the genital system	32 (4.8)	39 (0.8)	1.24	1.05
Urologicals	17 (2.6)	17 (0.3)	1.65	1.55
Musculoskeletal system	**230 (34.8)**	**308 (6.3)**	**11.22**	**9.62**
Antigout preparations	90 (13.6)	132 (2.7)	0.95	0.61
Anti-inflammatory and antirheumatic products	79 (12.0)	82 (1.7)	2.96	2.37
Drugs for treatment of bone diseases	92 (13.9)	92 (1.9)	7.28	6.61
Muscle relaxants	2 (0.3)	2 (0.0)	0.03	0.03
Nervous system	**339 (51.3)**	**575 (11.8)**	**36.93**	**30.67**
Analgesics	127 (19.2)	159 (3.3)	16.26	13.30
Antiepileptics	38 (5.7)	46 (0.9)	1.62	1.47
Anti-Parkinson drugs	11 (1.7)	16 (0.3)	1.23	1.11
Other nervous system drugs	2 (0.3)	2 (0.0)	0.37	0.25
Psychoanaleptics	205 (31.0)	223 (4.6)	10.83	9.03
Psycholeptics	109 (16.5)	129 (2.6)	6.62	5.52
Respiratory system	**179 (27.1)**	**281 (5.7)**	**22.06**	**20.17**
Antihistamines for systemic use	11 (1.7)	17 (0.3)	0.75	0.64
Cough and cold preparations	1 (0.2)	1 (0.0)	0.22	0.21
Drugs for obstructive airway diseases	169 (25.6)	258 (5.3)	20.94	19.19
Nasal preparations	5 (0.8)	5 (0.1)	0.16	0.13
Sensory organs	**94 (14.2)**	**128 (2.6)**	**4.69**	**3.72**
Ophthalmologicals	94 (14.2)	127 (2.6)	4.65	3.70
Otologicals	1 (0.2)	1 (0.0)	0.03	0.02
Systemic hormonal preparations, excl. sex hormones and insulins	**123 (18.6)**	**146 (3.0)**	**1.23**	**0.74**
Corticosteroids for systemic use	49 (7.4)	51 (1.0)	0.65	0.27
Thyroid therapy	81 (12.3)	95 (1.9)	0.58	0.47
Total	**(n=661)**	**4891 (100)**	**235.97**	**202.92**

*Assumes a patient contribution of $5 per item

6.2.2 Drug costs after HMR

The changes in drug costs resulting from the recommendations made by the pharmacists in the HMR reports were calculated in a two-stage process. Firstly, the changes resulting from every recommendation made by the pharmacists were calculated. The outcomes data (Section 5.4.6 of the previous chapter) was then used to calculate the changes in drug costs resulting from only the recommendations

implemented by the GP. By investigating the drug cost data in this way, both the *potential* (cost of implementing every recommendation) and *realised* (cost of only implemented recommendations) changes in drug therapy were analysed.

6.2.2.1 Drug costs after HMR if all recommended changes were implemented

Had all of the pharmacists' recommendations been accepted and implemented by the GP, changes in drug costs were expected to occur in 442 HMRs (66.9% of HMRs) to resolve or prevent 783 DRPs (33.7% of the total DRPs). At the baseline assumption of a $5 patient contribution per item, this was estimated to result in a non-significant net increase in drug costs of $1483.82 monthly ($17 806 annually), an average of $2.24 per HMR ($26.94 annually). A comparison between the estimated monthly drug costs before and after HMR is shown in Table 93.

TABLE 93 - COMPARISON BETWEEN ESTIMATED MONTHLY DRUG COSTS BEFORE AND AFTER HMR ASSUMING THAT ALL RECOMMENDATIONS WERE IMPLEMENTED

PARAMETER ($)	BEFORE HMR	AFTER HMR	WILCOXON SIGNED RANK TEST RESULT
Median cost [interquartile range]	165.88 [140.85]	168.20 [142.34]	*Z*=-0.653, *P*=0.514
Range	6.30 - 2060.99	0.08 - 2057.49	-
Total cost (661 HMRs)	136 380.48	137 864.31	-

The distribution of the monthly drug costs to the PBS per patient after the HMR had every recommendation been implemented is shown in Figure 40.

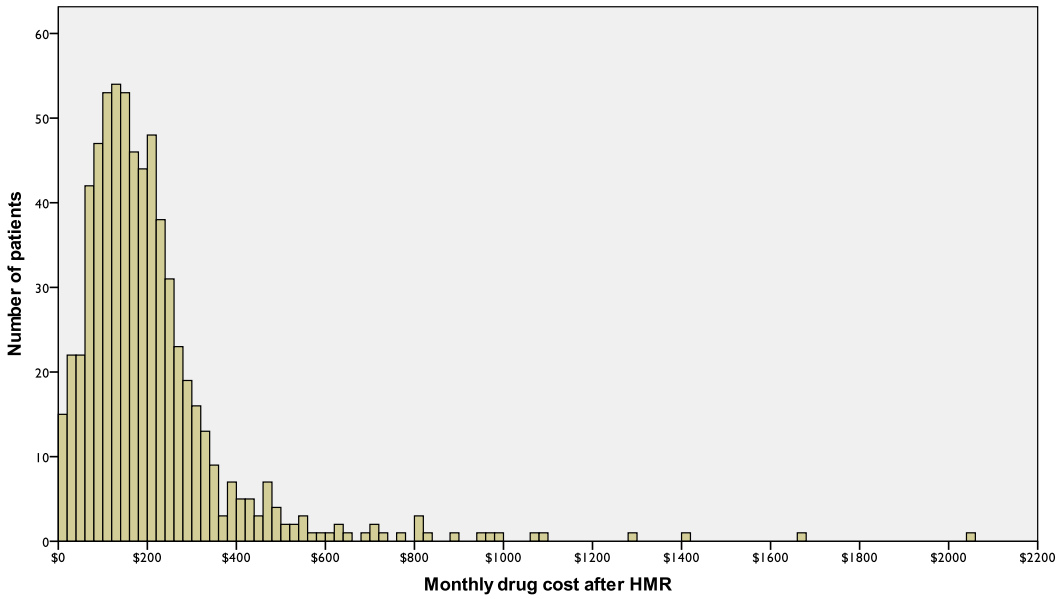

FIGURE 40 - DISTRIBUTION OF MONTHLY DRUG COSTS TO THE PBS PER PATIENT AFTER THE HMR BASED ON IMPLEMENTATION OF ALL RECOMMENDATIONS MADE IN THE HMR REPORT

The additional costs and savings differed markedly between the different groups of drugs. Table 94 shows the changes in monthly drug costs according to the various drug classes.

TABLE 94 - POTENTIAL CHANGES IN MONTHLY DRUG COSTS TO PBS ACCORDING TO DRUG CLASS BASED ON IMPLEMENTATION OF ALL RECOMMENDATIONS MADE IN THE HMR REPORT

DRUG CLASS (ATC LEVEL 1) ATC LEVEL 2	DRUGS STARTED		DRUGS CEASED		AVERAGE ADDITIONAL COST OR SAVING PER PATIENT ($)*
	NUMBER (% OF TOTAL PATIENTS)	AVERAGE COST PER PATIENT ($, N=661)	NUMBER (% OF TOTAL PATIENTS)	AVERAGE COST PER PATIENT ($, N=661)	
Alimentary tract and metabolism	**92 (14.9)**	**3.20**	**107 (17.2)**	**4.72**	**-1.52**
Antidiarrheals, intestinal antiinflammatory/antiinfective agents			1 (0.2)	0.05	-0.05
Drugs for acid related disorders	49 (7.9)	2.29	68 (10.9)	3.32	-1.03
Drugs for functional gastrointestinal disorders	5 (0.8)	0.04	1 (0.2)	0.02	0.02
Drugs used in diabetes	36 (5.8)	0.83	34 (5.5)	1.32	-0.49
Mineral supplements	1 (0.2)	0	2 (0.3)	0.01	-0.01
Vitamins	1 (0.2)	0.03	1 (0.2)	0	0.03
Antiinfectives for systemic use	**10 (1.6)**	**0.07**	**9 (1.4)**	**0.17**	**-0.10**
Antibacterials for systemic use	4 (0.6)	0.06	9 (1.4)	0.17	-0.11
Vaccines	6 (1.0)	0.01			0.01
Antineoplastic and immunomodulating agents	**1 (0.2)**	**0.21**	**2 (0.3)**	**0.02**	**0.19**
Immunosuppressants	1 (0.2)	0.21	2 (0.3)	0.02	0.19
Blood and blood forming organs	**58 (9.4)**	**2.61**	**38 (6.1)**	**1.06**	**1.55**
Antianaemic preparations	6 (1.0)	1.73	3 (0.5)	0.02	1.71
Antithrombotic agents	52 (8.4)	0.88	35 (5.6)	1.04	-0.16
Cardiovascular system	**237 (38.3)**	**8.04**	**209 (33.5)**	**6.73**	**1.31**
Agents acting on the renin-angiotensin system	69 (11.2)	1.83	56 (9.0)	1.59	0.24
Antihypertensives	2 (0.3)	0.02	7 (1.1)	0.05	-0.03
Beta blocking agents	20 (3.2)	0.44	17 (2.7)	0.41	0.03
Calcium channel blockers	34 (5.5)	0.7	27 (4.3)	0.65	0.05
Cardiac therapy	16 (2.6)	0.21	18 (2.9)	0.2	0.01
Diuretics	31 (5.0)	0.13	36 (5.8)	0.12	0.01
Lipid modifying agents	65 (10.5)	4.71	48 (7.7)	3.71	1.00
Genitourinary system and sex hormones	**8 (1.3)**	**0.22**	**11 (1.8)**	**0.29**	**-0.07**
Sex hormones and modulators of the genital system	5 (0.8)	0.21	6 (1.0)	0.18	0.03
Urologicals	3 (0.5)	0.01	5 (0.8)	0.11	-0.10
Musculo-skeletal system	**48 (7.8)**	**1.11**	**94 (15.1)**	**2.20**	**-1.09**
Antigout preparations	25 (4.0)	0.05	37 (5.9)	0.21	-0.16
Antiinflammatory and antirheumatic products	11 (1.8)	0.27	44 (7.1)	1.2	-0.93
Drugs for treatment of bone diseases	12 (1.9)	0.79	12 (1.9)	0.78	0.01
Muscle relaxants			1 (0.2)	0.01	-0.01
Nervous system	**123 (19.9)**	**4.05**	**113 (18.1)**	**2.90**	**1.15**

Drug class (ATC level 1) ATC level 2	Drugs started		Drugs ceased		Average additional cost or saving per patient ($)*
	Number (% of total patients)	Average cost per patient ($, n=661)	Number (% of total patients)	Average cost per patient ($, n=661)	
Analgesics	75 (12.1)	2.12	24 (3.9)	0.93	1.19
Antiepileptics	5 (0.8)	0.14	4 (0.6)	0.03	0.11
Anti-Parkinson drugs	2 (0.3)	0.63	2 (0.3)	0.16	0.47
Psychoanaleptics	29 (4.7)	1.1	53 (8.5)	1.56	-0.46
Psycholeptics	12 (1.9)	0.06	30 (4.8)	0.22	-0.16
Respiratory system	**34 (5.5)**	**2.34**	**24 (3.9)**	**1.36**	**0.98**
Antihistamines for systemic use	1 (0.2)	0.01	1 (0.2)	0	0.01
Drugs for obstructive airway diseases	33 (5.3)	2.33	23 (3.7)	1.36	0.97
Sensory organs	**5 (0.8)**	**0.15**	**8 (1.3)**	**0.20**	**-0.05**
Ophthalmologicals	5 (0.8)	0.15	8 (1.3)	0.2	-0.05
Systemic hormonal preparations, excl. sex hormones and insulins	**2 (0.3)**	**0.02**	**8 (1.3)**	**0.09**	**-0.07**
Corticosteroids for systemic use			3 (0.5)	0.01	-0.01
Thyroid therapy	2 (0.3)	0.02	5 (0.8)	0.08	-0.06
Total (661 HMRs)	**618 (100)**	**14 545.96**	**623 (100)**	**13 062.13**	**1 483.82**

Numbers in brackets show percentage of total; * Negative numbers denote savings

The drug class that most frequently would have resulted in a reduction to the monthly drug cost involved agents that reduce gastric acid production. Most commonly, these were proton pump inhibitors such as esomeprazole and pantoprazole. Psychoanaleptics (such as benzodiazepines and antidepressants) would also have resulted in frequent reductions in drug costs; however, as many of these medications were of relatively small cost, the effect of ceasing them on the total monthly drug cost was considerably less than that for proton pump inhibitors. Changes to the dose or cessation of anti-inflammatories, such as celecoxib, were frequent, and also resulted in a relatively high reduction in monthly drug cost.

The drug classes most frequently implicated in increasing the monthly drug costs were commenced to treat conditions which were frequently identified as undertreated, such as pain and risk factors for cardiovascular disease (predominantly hypertension and hyperlipidaemia). In contrast, drugs to treat anaemia were estimated to have contributed the most to increased monthly drug costs, mainly due to the relatively high monthly cost of preparations containing erythropoeitin.

6.2.2.2 Drug costs after HMR resulting from implemented changes

As shown in section 5.4.5, a proportion of the recommendations made by the pharmacists were not implemented by the GP following the HMR. The outcomes data was used to calculate the effect of the *implemented* changes on drug costs by costing only the recommendations that were either *Accepted* or *Partially accepted*. Of the 661 HMRs that were submitted for the study, outcomes data were provided for 560 (84.7%) of them. In these HMRs, recommendations made to resolve 341 DRPs were estimated to result in changes to drug costs in 249 HMRs (44.5%).

In contrast to the results of the previous section, the implemented changes were estimated to result in a net reduction in monthly drug costs of $700.93 ($8411 annually), an average of $1.25 per HMR ($15.02 annually). However, the difference in costs was again not significant (Table 95).

TABLE 95 - COMPARISON BETWEEN ESTIMATED MONTHLY DRUG COSTS BEFORE AND AFTER HMR COSTING ONLY IMPLEMENTED RECOMMENDATIONS

PARAMETER ($)	BEFORE HMR	AFTER HMR	WILCOXON SIGNED RANK TEST RESULT
Median cost [interquartile range]	162.38 [137.11]	161.10 [140.16]	Z=-1.622, P=0.105
Range	6.30 - 2060.99	0.08 - 2060.99	-
Total cost (560 HMRs)	116 430.49	115 729.56	-

Consistent with the results of the previous section, there were substantial differences in additional costs and savings between the different groups of drugs. The changes in monthly drug costs resulting from implemented recommendations according to the various drug classes are shown in Table 96.

TABLE 96 - POTENTIAL CHANGES IN MONTHLY DRUG COSTS TO PBS ACCORDING TO DRUG CLASS BASED ON RECOMMENDATIONS MADE IN THE HMR REPORT IMPLEMENTED FOLLOWING THE HMR

DRUG CLASS (ATC LEVEL 1) ATC LEVEL 2	DRUGS STARTED		DRUGS CEASED		AVERAGE ADDITIONAL COST OR SAVING PER PATIENT ($)*
	NUMBER (% OF TOTAL PATIENTS)	AVERAGE COST PER PATIENT ($, N=560)	NUMBER (% OF TOTAL PATIENTS)	AVERAGE COST PER PATIENT ($, N=560)	
Alimentary tract and metabolism	**35 (14.2)**	**1.34**	**46 (17.2)**	**2.10**	**-0.76**
Drugs for acid related disorders	16 (6.5)	0.96	25 (9.3)	1.39	-0.42
Drugs for functional gastrointestinal disorders	1 (0.4)	0.02	1 (0.4)	0.02	-0.01
Drugs used in diabetes	18 (7.3)	0.36	19 (7.1)	0.68	-0.33
Mineral supplements		0.00	1 (0.4)	0.01	-0.01
Antiinfectives for systemic use	**3 (1.2)**	**0.02**	**4 (1.5)**	**0.11**	**-0.09**
Antibacterials for systemic use	1 (0.4)	0.01	4 (1.5)	0.11	-0.10
Vaccines	2 (0.8)	0.00		0.00	0.00
Blood and blood forming organs	**26 (10.5)**	**0.06**	**8 (3.0)**	**0.21**	**-0.16**
Antianaemic preparations	1 (0.4)	0.00	1 (0.4)	0.00	0.00
Antithrombotic agents	25 (10.1)	0.05	7 (2.6)	0.21	-0.16
Cardiovascular system	**72 (29.1)**	**3.00**	**74 (27.6)**	**2.73**	**0.27**
Agents acting on the renin-angiotensin system	28 (11.3)	0.91	23 (8.6)	0.79	0.12
Antihypertensives	1 (0.4)	0.01	1 (0.4)	0.01	0.00
Beta blocking agents	7 (2.8)	0.27	4 (1.5)	0.18	0.09
Calcium channel blockers	9 (3.6)	0.26	9 (3.4)	0.24	0.03
Cardiac therapy	6 (2.4)	0.10	10 (3.7)	0.10	0.00
Diuretics	3 (1.2)	0.01	10 (3.7)	0.02	-0.01
Lipid modifying agents	18 (7.3)	1.44	17 (6.3)	1.40	0.04
Genito urinary system and sex hormones	**3 (1.2)**	**0.03**	**7 (2.6)**	**0.13**	**-0.10**
Sex hormones and modulators of the genital system	1 (0.4)	0.02	3 (1.1)	0.10	-0.08
Urologicals	2 (0.8)	0.01	4 (1.5)	0.03	-0.02
Musculo-skeletal system	**31 (12.6)**	**0.39**	**50 (18.7)**	**1.34**	**-0.95**
Antigout preparations	23 (9.3)	0.05	19 (7.1)	0.16	-0.11
Antiinflammatory and antirheumatic products	6 (2.4)	0.18	26 (9.7)	0.77	-0.60
Drugs for treatment of bone diseases	2 (0.8)	0.16	5 (1.9)	0.41	-0.25
Nervous system	**59 (23.9)**	**1.69**	**57 (21.3)**	**1.66**	**0.03**
Analgesics	35 (14.2)	1.26	8 (3.0)	0.66	0.60
Antiepileptics	3 (1.2)	0.07	1 (0.4)	0.01	0.06
Psychoanaleptics	13 (5.3)	0.30	33 (12.3)	0.84	-0.53
Psycholeptics	8 (3.2)	0.06	15 (5.6)	0.15	-0.10
Respiratory system	**14 (5.7)**	**1.20**	**12 (4.5)**	**0.63**	**0.57**
Drugs for obstructive airway diseases	14 (5.7)	1.20	12 (4.5)	0.63	0.57

Drug class (ATC level 1) ATC level 2	Drugs started		Drugs ceased		Average additional cost or saving per patient ($)*
	Number (% of total patients)	Average cost per patient ($, n=560)	Number (% of total patients)	Average cost per patient ($, n=560)	
Sensory organs	**3 (1.2)**	**0.11**	**6 (2.2)**	**0.16**	**-0.06**
Ophthalmologicals	3 (1.2)	0.11	6 (2.2)	0.16	-0.06
Systemic hormonal preparations, excl. sex hormones and insulins	**1 (0.4)**	**0.01**	**4 (1.5)**	**0.02**	**0.00**
Corticosteroids for systemic use		0.00	1 (0.4)	0.01	-0.01
Thyroid therapy	1 (0.4)	0.01	3 (1.1)	0.01	0.00
Total (560 HMRs)	**247 (100.0)**	**7.84**	**268 (100.0)**	**9.10**	**1.25**

Numbers in brackets show percentage of total; * Negative numbers denote savings

The differences between drug classes and the estimates of drug costs changes resulting from the HMRs in these two scenarios are illustrated in Figure 41 (drugs grouped by ATC level 1 codes) and Figure 42 (ATC level 2 grouping). Only HMRs for which outcomes data were available are represented in these figures (n=560). There were several differences in the proportions of cost changes between the two scenarios evident in several of the drug classes. In particular, the proportions of implemented recommendations that were estimated to increase drug costs appear lower than those that were estimated to decrease drug costs. This was consistent with the findings reported in section 5.4.6.1 that a greater proportion of recommendations to decrease doses or cease drugs were implemented compared to recommendations to increase doses or start new drugs.

In both figures, the increased cost for the ATC level 1 group *Blood and blood forming organs* is skewed by a recommendation to commence erythropoietin in a single HMR.

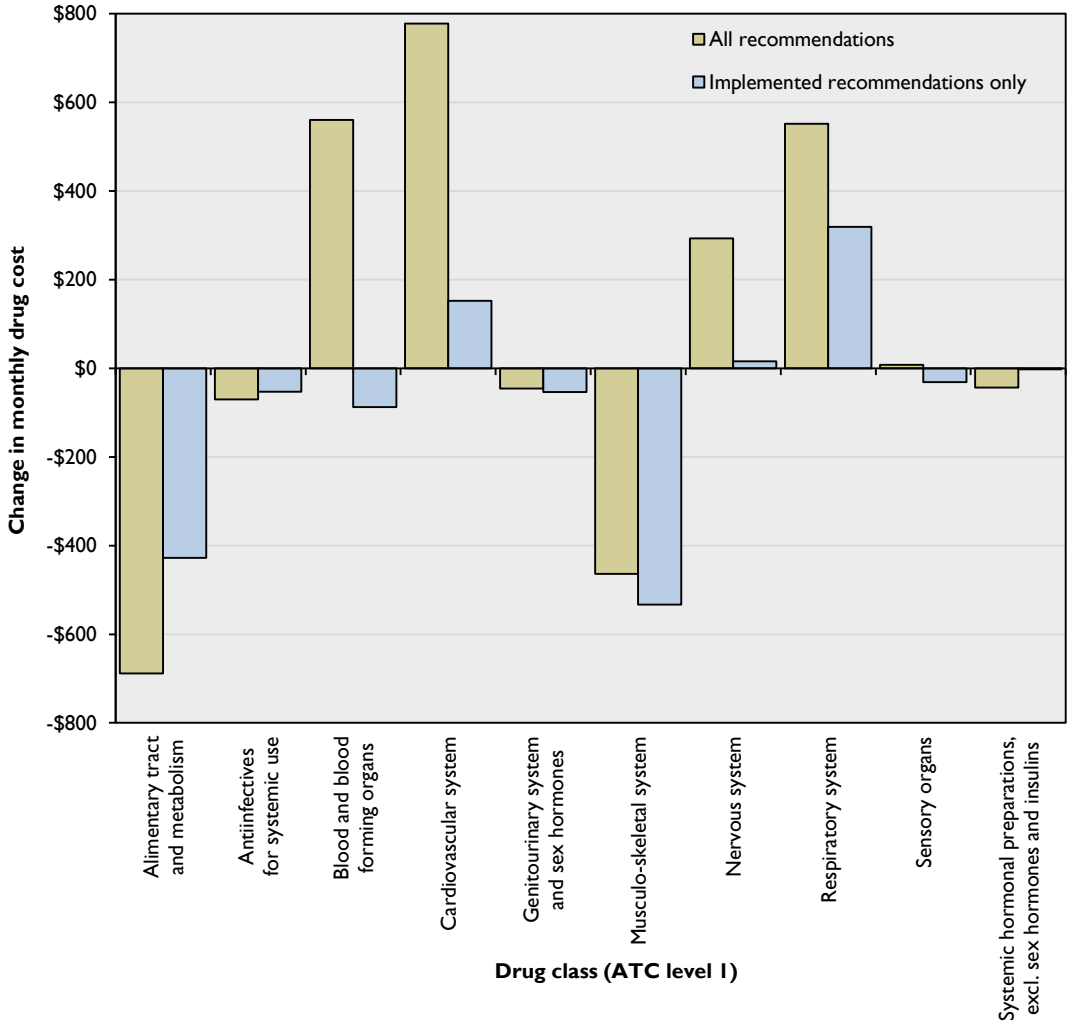

FIGURE 41 - DRUG COST CHANGES RESULTING FROM ALL RECOMMENDATIONS MADE COMPARED TO ONLY THOSE IMPLEMENTED FOLLOWING HMRS ACCORDING TO ATC LEVEL 1 GROUPING. NEGATIVE NUMBERS DENOTE SAVINGS.

Analysis of the drugs at ATC Level 2 grouping (Figure 42) provides further insight into the reasons for the differences in cost changes resulting from different drug types. For example, whilst many recommendations were made that would increase the cost of lipid lowering agents were they implemented, it appears that few of them were implemented as the actual cost increase is minor.

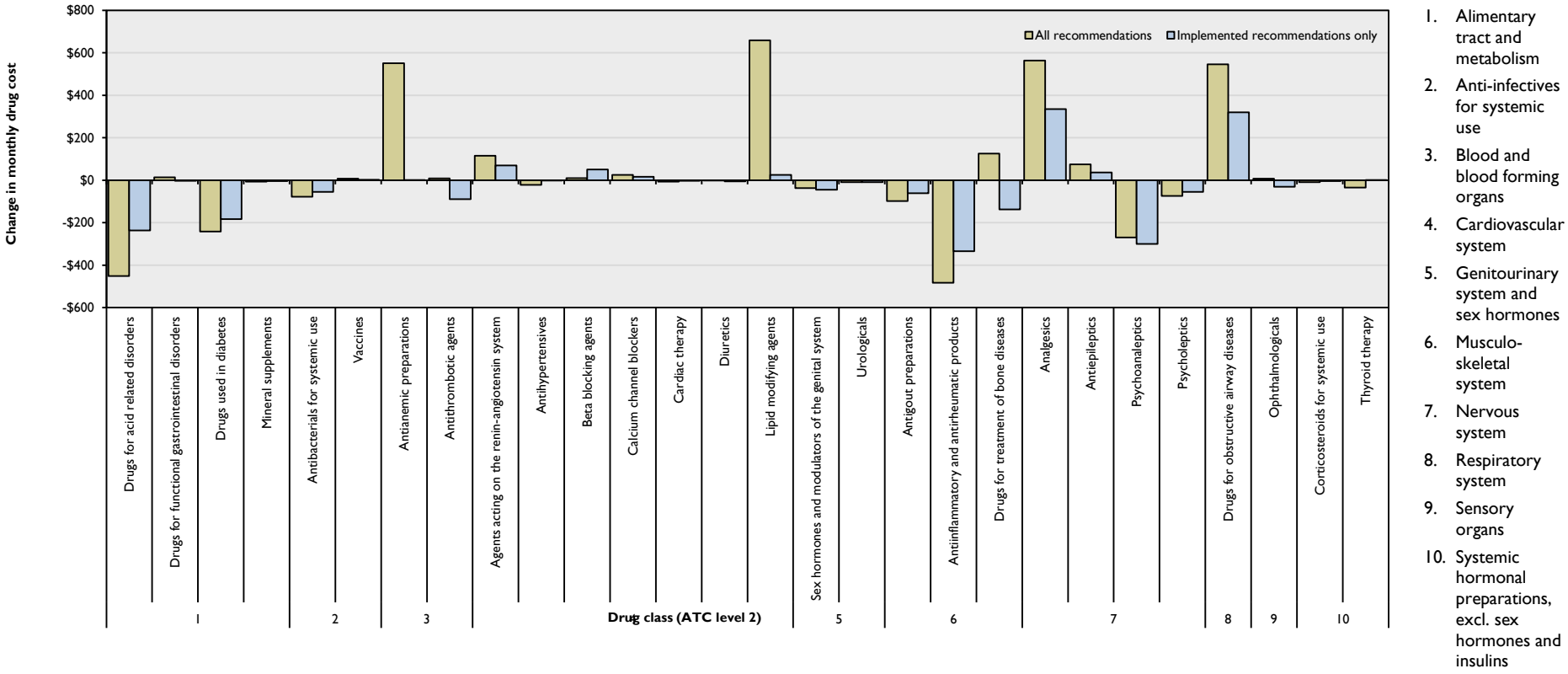

FIGURE 42 - DRUG COST CHANGES RESULTING FROM ALL RECOMMENDATIONS MADE COMPARED TO ONLY THOSE IMPLEMENTED FOLLOWING HMRS ACCORDING TO ATC LEVEL 2 GROUPING. NEGATIVE NUMBERS DENOTE SAVINGS.

In summary, it is apparent from these data that the HMRs were unlikely to have caused substantially increased or decreased drug costs. In addition, the changes in drug costs that did occur were not consistent across every drug group. The drug classes responsible for the greatest savings were those used to treat disorders of the *Musculoskeletal* and *Alimentary tract and metabolism*, and that responsible for the greatest increase in costs involved drugs that treat *Respiratory* system diseases.

6.3 Cost-consequence analysis - clinical outcomes and associated costs

Expert opinion was used to predict the potential clinical outcomes of a sample of the HMRs using the methodology described in section 2.6 of this thesis. The results of the studies described in Chapters 3 and 4 were then used to generate estimates of the costs, savings and QOL changes associated with these predicted clinical outcomes. Budgetary constraints prevented the entire dataset of 661 HMRs undergoing expert assessment to predict their potential clinical outcomes. A sample of 180 reviews was therefore selected from the 661 HMRs for analysis by a panel of 16 medication therapy experts. Each expert was allocated to one of four panels; each panel assessed 60 HMRs common to all four panels, and a further 30 that were unique to each panel.

6.3.1 Sampling considerations

During data entry of the 661 HMRs, it was noted that there was significant differences in the HMRs with regard to the amount of information contained in the referral. Some referrals contained detailed medical histories and extensive laboratory/pathology data; however, many did not. It was considered that the amount of information available in the referral may confound the results of the study in two ways, as follows:

- for the HMRs that had limited information available in the referral (providing less information to the pharmacist who performed the HMR), the recommendations made in the HMR may have been more generalised and therefore potentially less economically valuable, and
- provision of less information to the expert panels may adversely affect the validity of the assessment process, as more assumptions would have been made by the expert in their assessment.

To overcome this potential confounder, stratified random sampling was used to minimise any chance of differences between the sample of 180 HMRs for assessment and the remaining 661 reviews in this regard. As no formal criteria that classify the comprehensiveness of HMR referrals have been published, a simple classification scheme was devised for the sampling exercise. The referral information of the 661 HMRs was classified according to two aspects as follows:

- medical history, which was classified as either "detailed" or "minimal", and
- laboratory and pathology results, which were classified as either "recent and potentially relevant" or "irrelevant, limited or absent".

The criteria used to perform these classifications are shown in Table 97.

TABLE 97 - CRITERIA USED TO CLASSIFY HMR REFERRALS FOR STRATIFICATION

MEDICAL HISTORY	
Detailed	**Minimal**
• Multiple "active" diagnoses • Basic patient demographics (height, weight, blood pressure) provided	• No diagnoses listed • No "active" diagnoses • Basic patient demographics (height, weight, blood pressure) missing
PATHOLOGY / LABORATORY RESULTS	
Recent and potentially relevant	**Irrelevant, limited or absent**
• At least one panel of pathology data provided • Data from less than six months prior to the HMR	• No pathology / laboratory investigations provided • Handwritten summaries (for example, "*LFTs normal*") • All data from greater than six months prior to the HMR

The results of the stratification are shown in Table 98. Examples of each type of referral are shown in Appendix XX.

TABLE 98 - STRATIFICATION OF HMRS ACCORDING TO CONTENTS OF REFERRAL

NUMBER (%) OF TOTAL HMRS		PATHOLOGY RESULTS		
		Irrelevant, limited or absent	Recent and potentially relevant	TOTAL
Medical history	Detailed	126 (19.1)	185 (28.0)	**311 (47.0)**
	Minimal	177 (26.8)	173 (26.2)	**350 (53.0)**
TOTAL (n=661)		**303 (45.8)**	**358 (54.2)**	**661 (100)**

Of the 661 HMRs submitted for the study, no DRPs were documented in 18 of them (Section 5.4 page 225). As the expert assessment involved analysis of the recommendations made to resolve the DRPs identified in the HMRs, these 18 HMRs were excluded from the dataset, leaving 643 HMRs. One hundred and eighty HMRs were then randomly selected from the 643 HMRs according to the proportions in the above stratification by allocating each HMR a random number using the RAND function contained within Microsoft Excel 2010 (Microsoft Corporation, Redmond, WA, USA).

Methodological constraints necessitated the exclusion of the 18 HMRs in which no DRPs were documented prior to the sampling. However, it was inappropriate to exclude these HMRs from the economic analysis since costs were incurred by providing them. Consequently, these HMRs are accounted for in the analysis presented in Section 6.3.4.1.5.

The following section compares the characteristics of the sample of 180 HMRs used for the economic evaluation to those of the complete dataset of 661 HMRs.

6.3.2 Characteristics of the sample

6.3.2.1 General demographics

The sampling resulted in the selection of 180 HMRs undertaken by 101 different pharmacists (68% of participants). A comparison between the baseline characteristics of the patients in the panel-evaluated HMRs and the complete dataset is shown in Table 99.

TABLE 99 - COMPARISONS OF GENERAL DEMOGRAPHICS BETWEEN SAMPLED HMRS AND THE COMPLETE STUDY DATASET

CHARACTERISTIC (MEAN ±SD UNLESS STATED OTHERWISE)	SAMPLE (N=180)	TOTAL (N=661)	TEST RESULT	P- VALUE
Number (%) of males	72 (40.0)	278 (42.1)	χ^2=0.326, df=1*	0.557
Age (years)	77.0 ± 10.6	76.0 ± 10.4	*t*=1.21, df=179†	0.228
Number of medical conditions	9.0 ± 5.4	8.9 ± 5.1	*t*=0.277, df=179†	0.782
Number of total medications	12.8 ± 4.9	11.8 ± 4.5	*t*=2.774, df=179†	0.006
Number of regular medications	10.5 ± 3.9	9.6 ± 3.8	*t*=3.062, df=179†	0.003
Median (IQR) monthly cost to PBS of regular medications ($)	191.70 (146.61)	165.88 (140.85)	*Z*=2.689§	0.007
Number of DRPs identified per HMR	4.0 ± 1.7	3.5 ± 1.8	*t*=4.191, df=179†	<0.001

*χ^2 test for goodness of fit; †One sample t-test; §Mann-Whitney U test

From these results, some minor differences between the patients in the sampled HMRs and those in the complete dataset are apparent. Although the sample was taking a statistically significant different number of medications (approximately one more medication than the greater dataset with consequently greater monthly costs), the clinical significance of this difference is likely to be minimal. The difference in the mean number of DRPs per HMR is most likely due to the exclusion of the eighteen HMRs in which no DRPs were documented in the HMR report.

6.3.2.2 DRPs identified

Seven hundred and twenty-eight DRPs were identified in the 180 HMRs selected for the expert assessment. Outcomes data was collected for the first three issues identified in the HMR report (see Section 2.1.3.1), and the experts evaluated the first three DRPs that were documented in the pharmacist's HMR report. More than three DRPs were documented in 100 HMRs (55.6%), and six or more DRPs were documented in 31 (17.2%) of the HMRs that were selected for the expert assessment. Fewer than three DRPs were identified in 46 of the HMRs, resulting in the expert assessment of 487 individual DRPs (66.9% of the DRPs identified in the 180 HMRs). Outcomes data were provided for 160 of the 180 HMRs (88.9%).

The number and type of DRPs that were assessed by the expert panels are shown in Table 100. The total number of DRPs documented in the HMRs that were selected for the expert assessment and the complete dataset are also shown for comparison. A χ^2

test comparing the proportions of DRP types between the HMRs selected for the expert assessment and those that were not assessed identified significant differences between the groups (Pearson χ^2=23.9, df=7, *P*=0.001). Although a statistically significant difference between the groups was identified, there were no DRP types in which substantial discordance was noted. The DRP types in which the greatest differences were apparent were slightly higher proportions of *Non-clinical* and *Compliance* DRPs in the HMRs selected for the expert assessment compared to those that were not. However, the differences are small and unlikely to affect the validity of the results.

TABLE 100 - COMPARISON OF FREQUENCY OF DRPS TYPES BETWEEN HMRS ASSESSED BY EXPERT PANELS AND COMPLETE DATASET

DRP TYPE DRP SUBTYPE	NUMBER (%) OF DRPS		
	ASSESSED BY EXPERTS	IN HMRS ASSESSED BY EXPERTS	IN COMPLETE DATASET
Drug selection	**133 (27.3)**	**180 (24.7)**	**511 (22.0)**
Duplication	13 (2.7)	15 (2.1)	36 (1.5)
Drug interaction	38 (7.8)	53 (7.3)	189 (8.1)
Wrong drug			1 (0.0)
Wrong dosage form	2 (0.4)	2 (0.3)	3 (0.1)
Unnecessary therapy/no apparent current indication	36 (7.4)	49 (6.7)	132 (5.7)
Contraindications apparent	41 (8.4)	56 (7.7)	135 (5.8)
Other drug selection problem	3 (0.6)	5 (0.7)	15 (0.6)
Over or underdose prescribed	**43 (8.8)**	**60 (8.2)**	**198 (8.5)**
Dose too high	29 (6.0)	38 (5.2)	117 (5.0)
Dose too low	10 (2.1)	14 (1.9)	45 (1.9)
Other dose problem	4 (0.8)	8 (1.1)	36 (1.5)
Compliance & concordance	**51 (10.5)**	**90 (12.4)**	**321 (13.8)**
Taking too little	25 (5.1)	35 (4.8)	133 (5.7)
Taking too much	2 (0.4)	2 (0.3)	13 (0.6)
Difficulty using dosage form	8 (1.6)	12 (1.6)	40 (1.7)
Patient using out of date medication	3 (0.6)	4 (0.5)	16 (0.7)
Other compliance problem	13 (2.7)	37 (5.1)	119 (5.1)
Untreated indications	**143 (29.4)**	**207 (28.4)**	**638 (27.5)**
Condition not adequately treated	95 (19.5)	125 (17.2)	373 (16.1)
Therapy required	48 (9.9)	80 (11.0)	262 (11.3)
Other untreated indication problem		2 (0.3)	3 (0.1)
Monitoring	**40 (8.2)**	**72 (9.9)**	**238 (10.2)**
Laboratory monitoring	38 (7.8)	66 (9.1)	216 (9.3)
Non-laboratory monitoring	2 (0.4)	6 (0.8)	19 (0.8)

DRP TYPE DRP SUBTYPE	NUMBER (%) OF DRPS ASSESSED BY EXPERTS	IN HMRS ASSESSED BY EXPERTS	IN COMPLETE DATASET
Other monitoring problem			3 (0.1)
Education or information	**6 (1.2)**	**14 (1.9)**	**44 (1.9)**
Patient drug information request	1 (0.2)	1 (0.1)	6 (0.3)
Confusion about therapy	2 (0.4)	2 (0.3)	9 (0.4)
Demonstration of device	3 (0.6)	4 (0.5)	9 (0.4)
Disease management or advice		4 (0.5)	15 (0.6)
Other education or information problem		3 (0.4)	5 (0.2)
Non-clinical	**4 (0.8)**	**13 (1.8)**	**55 (2.4)**
Weight management problem			11 (0.5)
Dietary problem	1 (0.2)	4 (0.5)	13 (0.6)
Smoking problem		2 (0.3)	13 (0.6)
Alcohol problem	1 (0.2)	2 (0.3)	4 (0.2)
Other non-clinical problem	2 (0.4)	4 (0.5)	14 (0.6)
Toxicity or adverse reaction	**67 (13.8)**	**92 (12.6)**	**318 (13.7)**
Toxicity caused by dose	13 (2.7)	14 (1.9)	27 (1.2)
Toxicity caused by drug interaction	6 (1.2)		39 (1.7)
Toxicity evident	46 (9.4)		247 (10.6)
Other toxicity/adverse effect problem	2 (0.4)	2 (0.3)	5 (0.2)
Total	**487 (100)**	**728 (100)**	**2323 (100)**

6.3.2.3 Drug cost changes resulting from HMRs

A comparison between the drug costs changes occurring in the sample of 180 HMRs and the complete dataset of 661 HMRs is shown in Table 101.

TABLE 101 - DIFFERENCES IN DRUG COST CHANGES BETWEEN HMRS ASSESSED BY EXPERTS AND COMPLETE DATASET BASED ON IMPLEMENTATION OF ALL RECOMMENDATIONS MADE IN HMR REPORTS

DRUG CLASS (ATC LEVEL 1) ATC LEVEL 2	DRUGS STARTED				DRUGS CEASED				TOTAL ADDITIONAL AVERAGE COST OR SAVING PER PATIENT ($)*	
	NUMBER (% OF PATIENTS)		AVERAGE COST PER PATIENT ($)		NUMBER (% OF PATIENTS)		AVERAGE COST PER PATIENT ($)			
	SAMPLE†	ALL HMRS§	SAMPLE†	ALL HMRS§	SAMPLE†	ALL HMRS§	SAMPLE†	ALL HMRS§	SAMPLE†	ALL HMRS§
Alimentary tract and metabolism	**24 (11.3)**	**92 (14.9)**	**2.55**	**3.20**	**35 (16.1)**	**107 (17.2)**	**5.75**	**4.72**	**-3.20**	**-1.53**
Antidiarrhoeals, intestinal antiinflammatory/antiinfective agents			0.00	0.00		1 (0.2)	0.00	0.05	0.00	-0.05
Drugs for acid related disorders	11 (5.2)	49 (7.9)	1.77	2.29	22 (10.1)	68 (10.9)	3.87	3.32	-2.10	-1.03
Drugs for functional gastrointestinal disorders	1 (0.5)	5 (0.8)	0.01	0.04		1 (0.2)	0.00	0.02	0.01	0.02
Drugs used in diabetes	12 (5.6)	36 (5.8)	0.77	0.83	13 (6.0)	34 (5.5)	1.88	1.32	-1.12	-0.49
Mineral supplements		1 (0.2)	0.00	0.00		2 (0.3)	0.00	0.01	0.00	-0.01
Vitamins		1 (0.2)	0.00	0.03		1 (0.2)	0.00	0.00	0.00	0.03
Antiinfectives for systemic use	**4 (1.9)**	**10 (1.6)**	**0.06**	**0.07**	**3 (1.4)**	**9 (1.4)**	**0.25**	**0.17**	**-0.18**	**-0.11**
Antibacterials for systemic use	1 (0.5)	4 (0.6)	0.04	0.06	3 (1.4)	9 (1.4)	0.25	0.17	-0.20	-0.12
Vaccines	3 (1.4)	6 (1.0)	0.02	0.01			0.00	0.00	0.02	0.01
Antineoplastic and immunomodulating agents		**1 (0.2)**	**0.00**	**0.21**	**1 (0.5)**	**2 (0.3)**	**0.02**	**0.02**	**-0.02**	**0.19**
Immunosuppressants		1 (0.2)	0.00	0.21	1 (0.5)	2 (0.3)	0.02	0.02	-0.02	0.19
Blood and blood forming organs	**19 (8.9)**	**58 (9.4)**	**1.74**	**2.61**	**11 (5.1)**	**38 (6.1)**	**0.26**	**1.06**	**1.48**	**1.55**
Antianaemic preparations	1 (0.5)	6 (1.0)	0.01	1.73		3 (0.5)	0.00	0.02	0.01	1.71
Antithrombotic agents	18 (8.5)	52 (8.4)	1.72	0.88	11 (5.1)	35 (5.6)	0.26	1.04	1.47	-0.16

Drug class (ATC level 1) ATC level 2	Drugs started				Drugs ceased				Total additional average cost or saving per patient ($)*	
	Number (% of patients)		Average cost per patient ($)		Number (% of patients)		Average cost per patient ($)			
	Sample†	All HMRs§	Sample†	All HMRs§	Sample†	All HMRs§	Sample†	All HMRs§	Sample†	All HMRs§
Cardiovascular system	**94 (44.1)**	**237 (38.3)**	**12.03**	**8.04**	**79 (36.4)**	**209 (33.5)**	**9.97**	**6.73**	**2.06**	**1.30**
Agents acting on the renin-angiotensin system	22 (10.3)	69 (11.2)	2.11	1.83	17 (7.8)	56 (9.0)	1.81	1.59	0.29	0.24
Antihypertensives	1 (0.5)	2 (0.3)	0.02	0.02	3 (1.4)	7 (1.1)	0.09	0.05	-0.07	-0.03
Beta blocking agents	9 (4.2)	20 (3.2)	1.17	0.44	6 (2.8)	17 (2.7)	0.93	0.41	0.24	0.03
Calcium channel blockers	14 (6.6)	34 (5.5)	1.04	0.70	13 (6.0)	27 (4.3)	1.12	0.65	-0.08	0.04
Cardiac therapy	8 (3.8)	16 (2.6)	0.32	0.21	9 (4.1)	18 (2.9)	0.37	0.20	-0.05	0.01
Diuretics	10 (4.7)	31 (5.0)	0.18	0.13	10 (4.6)	36 (5.8)	0.14	0.12	0.04	0.01
Lipid modifying agents	30 (14.1)	65 (10.5)	7.19	4.71	20 (9.2)	48 (7.7)	5.50	3.71	1.69	0.99
Genitourinary system and sex hormones	**2 (0.9)**	**8 (1.3)**	**0.10**	**0.22**	**4 (1.8)**	**11 (1.8)**	**0.73**	**0.29**	**-0.64**	**-0.07**
Sex hormones and modulators of the genital system	1 (0.5)	5 (0.8)	0.08	0.21	2 (0.9)	6 (1.0)	0.39	0.18	-0.31	0.02
Urologicals	1 (0.5)	3 (0.5)	0.02	0.01	2 (0.9)	5 (0.8)	0.34	0.11	-0.32	-0.10
Musculoskeletal system	**14 (6.6)**	**48 (7.8)**	**0.95**	**1.11**	**30 (13.8)**	**94 (15.1)**	**2.36**	**2.20**	**-1.41**	**-1.09**
Antigout preparations	7 (3.3)	25 (4.0)	0.07	0.05	13 (6.0)	37 (5.9)	0.20	0.21	-0.13	-0.15
Antiinflammatory and antirheumatic products	5 (2.3)	11 (1.8)	0.38	0.27	14 (6.5)	44 (7.1)	1.58	1.20	-1.20	-0.94
Drugs for treatment of bone diseases	2 (0.9)	12 (1.9)	0.50	0.79	2 (0.9)	12 (1.9)	0.53	0.78	-0.03	0.01
Muscle relaxants			0.00	0.00	1 (0.5)	1 (0.2)	0.05	0.01	-0.05	-0.01
Nervous system	**48 (22.5)**	**123 (19.9)**	**7.08**	**4.05**	**43 (19.8)**	**113 (18.1)**	**4.50**	**2.90**	**2.58**	**1.15**
Analgesics	23 (10.8)	75 (12.1)	2.43	2.12	10 (4.6)	24 (3.9)	1.33	0.93	1.11	1.19

Drug class (ATC level 1) ATC level 2	Drugs started				Drugs ceased				Total additional average cost or saving per patient ($)*	
	Number (% of patients)		Average cost per patient ($)		Number (% of patients)		Average cost per patient ($)			
	Sample†	All HMRs§	Sample†	All HMRs§	Sample†	All HMRs§	Sample†	All HMRs§	Sample†	All HMRs§
Antiepileptics	3 (1.4)	5 (0.8)	0.46	0.14	2 (0.9)	4 (0.6)	0.09	0.03	0.36	0.11
Anti-Parkinson drugs	2 (0.9)	2 (0.3)	2.32	0.63	1 (0.5)	2 (0.3)	0.59	0.16	1.73	0.47
Psychoanaleptics	14 (6.6)	29 (4.7)	1.76	1.10	16 (7.4)	53 (8.5)	2.18	1.56	-0.42	-0.46
Psycholeptics	6 (2.8)	12 (1.9)	0.11	0.06	14 (6.5)	30 (4.8)	0.31	0.22	-0.20	-0.16
Respiratory system	**6 (2.8)**	**34 (5.5)**	**1.37**	**2.34**	**4 (1.8)**	**24 (3.9)**	**0.99**	**1.36**	**0.38**	**0.98**
Antihistamines for systemic use	1 (0.5)	1 (0.2)	0.05	0.01		1 (0.2)	0.00	0.00	0.05	0.01
Drugs for obstructive airway diseases	5 (2.3)	33 (5.3)	1.32	2.33	4 (1.8)	23 (3.7)	0.99	1.36	0.33	0.97
Sensory organs		**5 (0.8)**	**0.00**	**0.15**	**2 (0.9)**	**8 (1.3)**	**0.22**	**0.20**	**-0.22**	**-0.05**
Ophthalmologicals		5 (0.8)	0.00	0.15	2 (0.9)	8 (1.3)	0.22	0.20	-0.22	-0.05
Systemic hormonal preparations, excl. sex hormones and insulins	**2 (0.9)**	**2 (0.3)**	**0.06**	**0.02**	**5 (2.3)**	**8 (1.3)**	**0.28**	**0.09**	**-0.23**	**-0.07**
Corticosteroids for systemic use			0.00	0.00		3 (0.5)	0.00	0.01	0.00	-0.01
Thyroid therapy	2 (0.9)	2 (0.3)	0.06	0.02	5 (2.3)	5 (0.8)	0.28	0.08	-0.23	-0.06
Total	213 (100)	618 (100)	4 668.45 (100)	14 545.96 (100)	217 (100)	623 (100)	4 557.75 (100)	13 062.13 (100)	110.70	1 483.82

*Negative numbers denote savings; †n=180; §n=661. Numbers in brackets indicate percentage of total

Although some differences between the sampled HMRs and the complete dataset with regards to the changes occurring between the various drug classes were apparent, it appeared that most differences were likely to be of relatively minor significance. A Wilcoxon signed rank test identified no significant difference in the monthly drug costs before and after the HMRs in the sample of 180 HMRs (Table 102), which was consistent with the findings of the complete dataset. This analysis was repeated in the 160 sampled HMRs for which outcomes data were available. Based upon the recommendations that were actually implemented, a trend towards a slight increase in the median monthly drug costs following the HMR was found (P=0.008), although the magnitude of the difference was minimal.

TABLE 102 - COMPARISON BETWEEN ESTIMATED MONTHLY DRUG COSTS BEFORE AND AFTER HMR IN SAMPLE ASSESSED BY EXPERTS

PARAMETER ($)	BEFORE HMR	AFTER HMR	WILCOXON SIGNED RANK TEST RESULT
ALL RECOMMENDATIONS ACCEPTED (N=180)			
Median cost [interquartile range]	191.70 [146.61]	193.85 [135.83]	Z=0.056, P=0.955
Range	21.77 - 2060.99	0.37 - 2057.49	-
Total cost	41188.42	41299.12	-
IMPLEMENTED RECOMMENDATIONS ONLY (N=160)			
Median cost [interquartile range]	180.62 [143.67]	180.95 [145.39]	Z=-1.750, P=0.080
Range	21.77 - 2060.99	15.00 - 2060.99	-
Total cost	36007.78	35546.76	-

It was concluded from these analyses that the 180 sampled HMRs were generally representative of the 661 HMRs submitted for the study. Although some minor differences were observed, none were of a magnitude that warranted sample correction. It therefore seemed reasonable that the results of the expert panel assessment of the sample could be extrapolated to the greater dataset with some confidence.

6.3.3 Preliminary analysis of results of expert panel assessment

A panel of specialist and general medical practitioners, and hospital and community pharmacists was recruited in early 2009 to assess the sample of 180 HMRs according to the methodology outlined in Section 2.6.

6.3.3.1 Characteristics of the experts and number of HMRs assessed

The specialty and location of practice of the experts is shown in Table 103. Each expert had experience in Australian practice, with all but one currently practicing in Australia.

TABLE 103 - LOCATION OF PRACTICE AND SPECIALITY OF EXPERTS

TYPE	LOCATION OF PRACTICE	SPECIALTY (IF APPLICABLE)
General practitioner	New South Wales	n/a
	Queensland	
	Tasmania	
	Western Australia	
Specialist medical practitioner	New South Wales	Oncology
	South Australia	Endocrinology
	Sri Lanka	Clinical toxicology
	Tasmania	Endocrinology
	Tasmania	General medicine
	Tasmania	General medicine
	Western Australia	General medicine
Hospital pharmacist	Tasmania	n/a
	Tasmania	
Community pharmacist	Queensland	Medication review
	Western Australia	Medication review

The assessment process was conducted between May and July 2009. At this time, fourteen of the sixteen assessors had completed their assigned cases. Two of the consultant physicians withdrew from the study due to an inability to meet the study's

deadline for the HMR assessments.[xviii] One of these physicians had assessed thirteen HMRs, and the other had not commenced their assigned cases. The final numbers of HMRs assessed by each of the experts are shown in Table 104.

TABLE 104 - NUMBER OF HMRS ASSESSED BY PANELS OF EXPERTS

PANEL NUMBER	COMPOSITION	HMRS ASSESSED
One	Two specialists One GP One pharmacist	4 opinions on 3 unique HMRs 4 opinions on 10 common HMRs 3 opinions on 27 unique HMRs 3 opinions on 50 common HMRs
Two	Two specialists One GP One pharmacist	4 opinions on 30 unique HMRs 4 opinions on 60 common HMRs
Three	One specialist One GP One pharmacist	3 opinions on 30 unique HMRs 3 opinions on 60 common HMRs
Four	Two specialists One GP One pharmacist	4 opinions on 30 unique HMRs 4 opinions on 60 common HMRs

6.3.3.2 Consequences selected

The number of times each consequence was selected by the experts is shown in Table 105. The consequence most frequently selected was *Pain*, which accounted for approximately 8% of all of the consequences selected. Interestingly, the option of *No consequence* was selected almost as often as *Pain*, perhaps indicative of the frequency of minor interventions. *No consequence* was selected by every expert for 86 of the 487 DRPs (17.7%). In the 401 DRPs for which a consequence was selected by at least one of the experts, the mean number of consequences selected per DRP was 1.4 (±0.55 st dev).

[xviii] The outbreak of human swine influenza significantly impacted on one assessor's workload; the other assessor took sabbatical leave in a location without reliable internet access and was unable to complete the cases they had been assigned. Neither expert informed the researcher about these issues until the end of the data collection period; consequently, there was no opportunity to recruit replacement experts

It is notable that there were substantial differences between the experts regarding to the number of consequences they selected. For example, Expert 19 selected a total of 9 consequences for the entire assessment process; similarly, expert 17 selected a total of 59 consequences.[xix] In contrast, experts 10, 18 and 22 indicated that the interventions were potentially of *No consequence* much less frequently.

The only consequence not selected by any of the experts was *Gastrointestinal discomfort*.

TABLE 105 - NUMBER OF TIMES CONSEQUENCES SELECTED BY EXPERTS ASSESSING HMRS

CONSEQUENCE	NUMBER OF TIMES CONSEQUENCE SELECTED															TOTAL (% OF CONSEQUENCES SELECTED)
EXPERT TYPE	GP				PHARMACIST				SPECIALIST							
EXPERT	15	18	19	20	21	22	23	24	9*	10	12	13	14	16	17	
Acidosis	1	9		5	8	3	3	3	1	6	6	1	5	3		**54 (2.4)**
Alkalosis					1		2									**3 (0.1)**
Allergic reaction		1			1		1			9				1		**13 (0.6)**
Anaemia		11		1	5	1		9	1	2	5		1			**36 (1.6)**
Anxiety	2			1	2	1	1			2			2	1		**12 (0.5)**
Arrhythmia	1	11	2	8	8	6	4	11		17	9	3		7	4	**91 (4.0)**
Asthma	6	1		12	2	2	4	1		5	2				1	**36 (1.6)**
Bleeding, non-specific	1	8	1	8	10	14	1	9	4	9	2	13	3	8	1	**92 (4.0)**
Bone marrow suppression		1				2		2		1				1		**7 (0.3)**
Cerebrovascular event	19	13		7	17	7	3	9	1	17	2	5	4	1		**105 (4.6)**
Chronic airways disease	7	4			12	6	5	11			3	1	1		1	**51 (2.2)**
CNS Depression		2			2	9		1	2	4				1	1	**22 (1.0)**
Confusion	13	9		2	8	3	3	8	1	25	15	1	1	2		**91 (4.0)**
Constipation	5	26		5	8	9	2	5	1	12	4	3	11	5	1	**97 (4.2)**
Dementia		2			2	1										**5 (0.2)**
Depression	6	4		3	3			4	1	4	3	1	2		1	**32 (1.4)**
Diabetes	7	1		9	7	2	2	6		6	4	2	6		2	**54 (2.4)**
Diarrhoea	4	4		3	3	8	4	2		7	3		5	6	1	**50 (2.2)**

[xix] These experts were asked to clarify their responses as it was thought that the data collection system may not have recorded them correctly. The experts asserted that they had indeed selected *No consequence* frequently as they considered the majority of the interventions to be of such limited clinical significance that the before- and after- HMR probabilities of any consequence occurring was essentially nil

Consequence	**Number of Times Consequence Selected**															**Total (% of consequences selected)**
Expert type	**GP**				**Pharmacist**				**Specialist**							
Expert	**15**	**18**	**19**	**20**	**21**	**22**	**23**	**24**	**9***	**10**	**12**	**13**	**14**	**16**	**17**	
Gastrointestinal bleeding	25	20		8	11	1	1	10	7	2	19	1	1	1	5	**112 (4.9)**
Glaucoma	1				1				1							**3 (0.1)**
Headache	1	3				1							1		1	**7 (0.3)**
Heart failure	4	3		3	5	5	3	5	1	14	5	1	5	1	4	**59 (2.6)**
Hypercalcaemia		1		2	1	1	1			1	2					**9 (0.4)**
Hyperkalaemia		7	1	4	3	3	2	6	2	10	6	1		1	2	**48 (2.1)**
Hypertension	12	7		10	10	17	4	5	5	7	4	2	3	4	4	**94 (4.1)**
Hyperthyroidism					1	1	2			1		1				**6 (0.3)**
Hypocalcaemia											4	1				**5 (0.2)**
Hypoglycaemia	4	9	1	3	6	6	2	3	3	9	8	4	3	5	3	**69 (3.0)**
Hypokalaemia		11	1	1	1	3	2			5	2	3			3	**32 (1.4)**
Hypotension	1	16		7	6	8	2	5	3	6	7	2	10	13	3	**89 (3.9)**
Hypothyroidism		1			2	1	3	1		2		1				**11 (0.5)**
Infection, general		3			1	5		4		2						**15 (0.7)**
Insomnia	4	5		4	3	3	2	3	2			1	3		1	**31 (1.4)**
Liver disease	2	8		3	8	2	1	1		1	1				3	**30 (1.3)**
Myocardial ischaemia	26	11		23	30	14	8	18	3	24	3	7	9			**176 (7.7)**
Myopathy	5	7		5	7	6	1	10	4	8	13	8		1	5	**80 (3.5)**
Nausea				1	1	4		1	2	6		2		5	2	**24 (1.1)**
Oedema	2	8	1	3	3	10	1	7	1	7	1	3	3			**50 (2.2)**
Osteoporosis		15	1	10	13	12	11	22	1	15	1	2		1		**104 (4.6)**
Pain	17	11		13	27	14	11	28	9	22	11	8	1	2	5	**179 (7.8)**
Parkinsonism		1				5				2						**8 (0.4)**
Psychosis										1						**1 (0.0)**
Rash		2			6	3		3		1	2		1	1	1	**20 (0.9)**
Renal dysfunction	12	23	1	11	10	9	5	5	3	14	13	5	4	6	3	**124 (5.4)**
Respiratory depression		4			1			2		6	1					**14 (0.6)**
Seizures		1			1					1		1				**4 (0.2)**
Serotonin toxicity				1	3			3		4	1		1	1		**14 (0.6)**
Urinary incontinence				1	1		2							1		**5 (0.2)**
Urinary retention				1					1			1		3	1	**7 (0.3)**
Urinary tract infection	1									1						**2 (0.1)**
Total	**189**	**284**	**9**	**178**	**261**	**208**	**99**	**223**	**60**	**298**	**162**	**85**	**86**	**82**	**59**	**2283 (100)**
No consequence	118	83	262	105	71	109	161	112	4	84	117	176	198	194	201	1995

* Did not complete HMR assessment

The differences between the experts in terms of the consequences they selected for each DRP were particularly apparent when their individual assessments of the 60

HMRs assessed by every expert were analysed. In the 165 DRPs assessed by the experts in these HMRs, there was 100% agreement between the experts in only three DRPs (1.8%); each time the option of "No consequence" was selected. Two or more experts select at least one of the same consequences in 106 DRPs (64.2%). However, for the majority of these DRPs (64, 60.4%) only a single consequence was selected by two or more experts (Table 106).

TABLE 106 - NUMBER OF DRPS IN WHICH TWO OR MORE EXPERTS SELECTED THE SAME CONSEQUENCE/S IN THE SUBSET OF 60 HMRS ASSESSED BY EVERY EXPERT

NUMBER OF CONSEQUENCES SELECTED BY 2 OR MORE EXPERTS	NUMBER OF DRPS (N=165)
1	64
2	15
3	10
4	12
5	3
6	2
Number of DRPs where "No consequence" selected by 2 or more experts	140

In the 106 DRPs where at least two experts selected the same consequence (excluding those that selected "*No consequence*") most frequently only two of the experts did so (Table 107).

TABLE 107 - NUMBER OF EXPERTS THAT SELECTED THE SAME CONSEQUENCE/S IN DRPS WHERE AT LEAST TWO EXPERTS SELECTED THE SAME CONSEQUENCE (SUBSET OF 60 HMRS ASSESSED BY EVERY EXPERT)

NUMBER EXPERTS THAT SELECTED THE SAME CONSEQUENCE	NUMBER OF DRPS (N=106)*
2	69
3	43
4	25
5	18
6	15
7	12
8	6
9	7
10	4

* Column totals greater than 106 as common consequences occurred in multiple DRPs

From the data presented in this section, it is apparent that there was very limited agreement between the experts with regard to the consequences they selected. This resulted in substantial variation between their estimates of the costs and QOL effects of the HMRs, and profoundly affected the subsequent analysis (further detail is presented in Section 6.3.3.6). Furthermore, it was not possible to define distributions for the probabilities of each consequence from the experts' responses as initially planned, since for each DRP there was insufficient experts who selected the same consequence to undertake distribution fitting. Consequently, for each DRP, simple averages of the probability estimates given by each expert who selected the consequence were used to calculate the cost and QOL changes resulting from the HMRs.

6.3.3.3 HMRs with insufficient information to assess

If an expert considered that there was insufficient information to accurately assess a particular DRP, they were able to indicate that this was the case and not assign consequences and probabilities to that DRP. Whilst the experts were discouraged from using this option, it was used by six experts, as shown in Table 108. Interestingly, two of the pharmacist experts utilised this option far more frequently than any of the remaining experts.

TABLE 108 - NUMBER OF DRPS NOT ASSESSED BY EXPERTS DUE TO INSUFFICIENT INFORMATION

EXPERT TYPE	EXPERT	NUMBER OF DRPS (% OF TOTAL)	
		NOT ASSESSED	TOTAL
GP	15	0 (0.0)	242
	18	4 (1.6)	248
	19	0 (0.0)	250
	20	0 (0.0)	242
Pharmacist	21	7 (2.9)	242
	22	27 (10.9)	248
	23	0 (0.0)	250
	24	29 (12.0)	242
Specialist	9	0 (0.0)	36
	10	0 (0.0)	248
	12	1 (0.4)	238
	13	0 (0.0)	242
	14	0 (0.0)	248
	16	0 (0.0)	250
	17	1 (0.4)	242
TOTAL		**69**	

6.3.3.4 Number of beneficial and deleterious consequences selected

The expert assessment process involved them indicating whether beneficial or deleterious effects would potentially result from the recommendations made by the pharmacists to resolve the DRPs reported in the HMRs. Benefits were indicated by a decrease in the probability of a consequence occurring following the HMR, and deleterious effects by an increase in the probability.

The number of times each expert indicated that benefits and detriments would result from the HMRs is shown in Table 109. Overall, beneficial consequences were predicted to occur approximately twice as frequently as detrimental ones.

TABLE 109 - NUMBER OF TIMES EACH EXPERT INDICATED BENEFIT OR DETRIMENT RESULTING FROM HMRS

		NUMBER OF BENEFICIAL AND DETRIMENTAL CONSEQUENCES SELECTED AT DIFFERENT SEVERITY LEVELS *								
		MILD SEVERITY LEVEL			MODERATE SEVERITY LEVEL			SEVERE SEVERITY LEVEL		
EXPERT TYPE	EXPERT	DETRIMENT	BENEFIT	NIL EFFECT	DETRIMENT	BENEFIT	NIL EFFECT	DETRIMENT	BENEFIT	NIL EFFECT
GP	15	44 (24.0)	139 (76.0)	124	46 (24.6)	141 (75.4)	120	42 (23.2)	139 (76.8)	126
	18	99 (36.8)	170 (63.2)	98	99 (36.9)	169 (63.1)	99	38 (26.0)	108 (74.0)	221
	19	1 (11.1)	8 (88.9)	262	1 (14.3)	6 (85.7)	264	(0.0)	7 (100.0)	264
	20	21 (12.0)	154 (88.0)	108	22 (12.4)	155 (87.6)	106	23 (13.2)	151 (86.8)	109
Pharmacist	21	49 (18.9)	210 (81.1)	73	49 (19.0)	209 (81.0)	74	43 (19.6)	176 (80.4)	113
	22	44 (21.6)	160 (78.4)	113	43 (21.3)	159 (78.7)	115	31 (19.0)	132 (81.0)	151
	23	3 (11.1)	24 (88.9)	233	9 (11.8)	67 (88.2)	184	1 (14.3)	6 (85.7)	253
	24	43 (19.5)	177 (80.5)	115	40 (21.2)	149 (78.8)	145	27 (23.9)	86 (76.1)	220
Specialist	9	23 (41.8)	32 (58.2)	9	23 (41.1)	33 (58.9)	8	21 (38.2)	34 (61.8)	9
	10	46 (21.0)	173 (79.0)	163	51 (17.9)	234 (82.1)	98	38 (17.2)	183 (82.8)	160
	12	47 (29.7)	111 (70.3)	121	44 (28.0)	113 (72.0)	122	41 (28.9)	101 (71.1)	137
	13	52 (61.2)	33 (38.8)	176	52 (61.2)	33 (38.8)	176	52 (61.2)	33 (38.8)	176
	14	42 (52.5)	38 (47.5)	204	45 (54.2)	38 (45.8)	201	44 (53.7)	38 (46.3)	202
	16	78 (97.5)	2 (2.5)	196	79 (97.5)	2 (2.5)	195	80 (97.6)	2 (2.4)	194
	17	54 (91.5)	5 (8.5)	201	53 (91.4)	5 (8.6)	202	46 (88.5)	6 (11.5)	208
TOTAL		**646 (31.0)**	**1436 (69.0)**	**2196**	**656 (30.2)**	**1513 (69.8)**	**2109**	**527 (30.5)**	**1202 (69.5)**	**2543**

* Numbers in brackets indicate the percentage of each expert's responses at each severity level

The total number of consequences at the *Severe* level is less than that for the *Mild* and *Moderate* levels due to several experts indicating a zero probability of the selected consequence/s occurring at the higher severity level

It is noteworthy that four of the seven specialists (Experts 13, 14, 16 and 17) selected detrimental consequences more frequently than beneficial consequences at each severity level. This was contrary to the responses of the remaining experts, who generally indicated the HMRs would be of benefit much more frequently than cause detriment.

6.3.3.5 Attribution

To address the potential that another health professional may have intervened and resolved a particular DRP, each expert was asked to estimate the likelihood of this occurring for every DRP (termed *attribution*). The scale for attribution estimates ranged from 0 to 100%, where an attribution of 100% indicated that there was no likelihood of another party resolving the DRP.

The differences between the experts with regards to their estimates of the attribution to the pharmacist were investigated by comparing the mean attribution assigned to the DRPs in the 60 common HMRs. Summary statistics illustrating the differences between the individual and types of experts are shown in Table 110.

The data presented in Table 110 illustrates a broad spread of the estimates of attribution between the experts. One-way ANOVA analysis identified significant differences between the three groups ($F(2,2284)=149.15$, $P<0.001$. Post-hoc comparisons using the Tukey HSD test indicated that he mean of the pharmacists' estimates was significantly higher than those of either the GPs (difference in means 28.6, $P<0.001$) and the specialists (difference in means 21.9, $P<0.001$). Furthermore, the mean of the GP's estimates was significantly less than that of the specialists (difference in means 6.8, $P<0.001$). Given that the experts were aware that they were assessing interventions made by pharmacists, it is probably unsurprising that the pharmacists rated the attribution higher than either of the groups of doctors. It is possible that the GPs gave lower attribution scores as they considered that other health professionals (perhaps GPs) would be likely to identify the same DRPs as those identified by the pharmacists.

TABLE 110 - MEAN ATTRIBUTION VALUES ASSIGNED BY DIFFERENT TYPES OF EXPERTS FOR 60 HMRS ASSESSED BY EVERY EXPERT

EXPERT TYPE	EXPERT	ESTIMATED ATTRIBUTION	
		MEAN (SD)	RANGE (MIN - MAX)
GP	15	39.0 (20.9)	5 - 100
	18	29.9 (16.8)	2 - 70
	19	88.2 (4.5)	70 - 95
	20	16.1 (16.9)	1 - 100
	Total	**43.4 (31.5)**	**1 - 100**
Pharmacist	21	37.1 (26.7)	1 - 99
	22	65.8 (21.3)	5 - 95
	23	89.6 (16.6)	20 - 100
	24	97.8 (9.7)	30 - 100
	Total	**72.0 (30.9)**	**1 - 100**
Specialist	9 *	73.8 (14.8)	50 - 95
	10	64.0 (19.4)	0.111 - 90
	12	63.3 (29.7)	2 - 100
	13	50.7 (26.7)	10 - 90
	14	5.8 (2.3)	1 - 15
	16	50.1 (26.2)	5 - 99
	17	63.6 (26.1)	5 - 100
	Total	**50.2 (31.1)**	**0.111 - 100**
TOTAL		**54.1 (33.2)**	**0.111-100**

* Did not complete HMR assessment

As there was substantial variation between the experts in their attribution estimates, the uncertainty for this parameter for each DRP was investigated. For the 165 DRPs in the 60 common HMRs, the best-fit function included in the software program @RISK was used initially to identify the most appropriate distribution and its descriptive parameters (described in Section 2.6.4). Beta distributions were calculated for the attribution estimates for DRPs that a best-fit distribution could not be identified, and simple averages were used when a beta distribution could not be calculated. For the remaining 322 DRPs in the 120 panel-specific HMRs, there were only three or four attribution estimates for each DRP, which was insufficient data for the @RISK best-fit function to be used. Consequently, beta distributions were calculated for the attribution estimates for these DRPs, and simple averages were used when a beta distribution could not be calculated.

The results of the distribution fitting are shown in Table 111. The low number of best-fit distributions is further illustrative of the substantial variability between the experts previously observed.

TABLE 111 - RESULTS OF DISTRIBUTION FITTING FOR EXPERT ESTIMATES OF ATTRIBUTION FOR DRPS IN SAMPLED HMRS

DRP	DISTRIBUTION			
	BEST-FIT BETA	CALCULATED BETA	SIMPLE AVERAGE	TOTAL
Common HMRs	11	154	0	**165**
Panel specific HMRs	0	314	8	**322**
Total	**11**	**468**	**8**	**487**

The estimates of attribution and their uncertainty were subsequently used in the calculation of the potential clinical and economic outcomes of the HMRs described in section 6.3.4.

6.3.3.6 Reliability between panels

As previously outlined, each expert was assigned to one of four panels. Each panel assessed 90 HMRs; 60 common to all panels and a further 30 that only that panel assessed, so that a total of 180 HMRs were assessed. An important consideration for the results to be reliable using this approach was that consistency between the panels with regard to their assessment of the 60 common HMRs was required. If substantial differences were found between the panels in their estimates of the outcomes of the 60 common HMRs, then it was inappropriate to consider the estimates of the outcomes of the HMRs unique to each panel to be comparable. It was therefore necessary to investigate the reliability between the four panels' assessments of the 60 common HMRs.

To undertake this analysis, "raw estimates" of the before- and after- HMR QOL and costs were calculated for i) each expert, and ii) each panel for the 60 common HMRs. The raw estimate was calculated by considering only the consequences selected by each expert and their estimates of the before- and after-HMR probabilities of the consequences occurring, and was therefore indicative of the expert's opinion of the clinical content of the HMRs. Their estimates of attribution and uptake of the

pharmacist's recommendations were not included since these parameters were not directly related to the clinical content of the HMRs. Similarly, drug costs and the cost of each HMR were also not considered.

Each expert's raw estimates of the cost and QOL changes occurring in the 60 common HMRs are shown in Table 112.

TABLE 112 - INDIVIDUAL EXPERT RAW ESTIMATES OF HEALTHCARE COST AND QOL CHANGES OCCURRING IN THE 60 HMRS ASSESSED BY EACH EXPERT

EXPERT TYPE	EXPERT	HMRS ASSESSED	RAW ESTIMATED TOTAL (AVERAGE PER HMR)					
			BEFORE HMR		AFTER HMR		DIFFERENCE*	
			COSTS ($)	QOL (QALY)	COSTS ($)	QOL (QALY)	COSTS ($)	QOL (QALY)
GP	15	60	43794.92 (729.92)	1.172 (0.020)	38734.52 (645.58)	1.030 (0.017)	-5060.40 (-84.34)	-0.142 (-0.002)
	18	60	81302.11 (1355.04)	1.952 (0.033)	45171.69 (752.86)	1.110 (0.018)	-36130.42 (-602.17)	-0.842 (-0.014)
	19	60	5422.04 (90.37)	0.070 (0.001)	506.82 (8.45)	0.004 (0.000)	-4915.22 (-81.92)	-0.066 (-0.001)
	20	60	21385.50 (356.43)	0.441 (0.007)	19175.21 (319.59)	0.403 (0.007)	-2210.29 (-36.84)	-0.038 (-0.001)
Pharmacist	21	60	24664.59 (411.08)	0.837 (0.014)	20117.28 (335.29)	0.680 (0.011)	-4547.31 (-75.79)	-0.157 (-0.003)
	22	60	35671.02 (594.52)	0.787 (0.013)	25640.44 (427.34)	0.576 (0.010)	-10030.58 (-167.18)	-0.211 (-0.004)
	23	60	9068.89 (151.15)	0.231 (0.004)	3611.39 (60.19)	0.096 (0.002)	-5457.50 (-90.96)	-0.135 (-0.002)
	24	60	27116.26 (459.60)	0.821 (0.014)	15283.20 (259.04)	0.465 (0.008)	-11833.06 (-200.56)	-0.355 (-0.006)
Specialist	9	10	9289.27 (928.93)	0.294 (0.029)	7899.41 (789.94)	0.238 (0.024)	-1389.85 (-138.99)	-0.056 (-0.006)
	10	60	64331.34 (1072.19)	1.777 (0.030)	50663.03 (844.38)	1.329 (0.022)	-13668.30 (-227.81)	-0.449 (-0.007)
	12	60	59706.86 (995.11)	1.692 (0.028)	39893.88 (664.90)	1.176 (0.020)	-19812.99 (-330.22)	-0.516 (-0.009)
	13	60	8694.14 (144.90)	0.239 (0.004)	11071.03 (184.52)	0.283 (0.005)	2376.88 (39.61)	0.044 (0.001)
	14	60	31694.97 (528.25)	0.528 (0.009)	31208.16 (520.14)	0.597 (0.010)	-486.82 (-8.11)	0.070 (0.001)
	16	60	5543.63 (92.39)	0.125 (0.002)	13692.07 (228.20)	0.298 (0.005)	8148.44 (135.81)	0.173 (0.003)
	17	60	3632.60 (60.54)	0.113 (0.002)	8262.76 (137.71)	0.356 (0.006)	4630.16 (77.17)	0.243 (0.004)

* Negative numbers denote savings or gained QOL

From the data presented in this table, it is evident that there was substantial variation between the individual experts' estimates of the total health resource utilisation changes resulting from the 60 HMRs, which ranged from an increase in costs of $8148, to savings of $36 130! Interestingly, the raw estimates of every pharmacist and GP predicted savings to the health system and improved QOL. In contrast, several of the specialists predicted that the HMRs would increase healthcare costs and reduce QOL. The extreme disparity between the individual experts' estimates was somewhat similar to the results reported by Tenni.[204] In that study, the experts' individual estimates of average total savings to the healthcare system per intervention ranged from $60 to $1235.

In consideration of these results, it was probable that combining the individual experts' opinions into the panels designated *a priori* would not produce consistent results between the panels. This was indeed the case. Table 113 shows the raw estimated changes in costs and QOL for each panel in the 60 common HMRs. These raw estimates were calculated by averaging the estimated probabilities of each consequence indicated by the experts in each panel, and then multiplying these probability estimates by the appropriate values in the consequence table. Whilst each panel estimated that the 60 HMRs would result in savings to the healthcare system, the range of these estimates varied 20-fold.

TABLE 113 - EXPERT PANEL RAW ESTIMATES OF HEALTHCARE COST CHANGES OCCURRING IN THE 60 HMRS ASSESSED BY EACH EXPERT

PANEL	EXPERTS	TOTAL (AVERAGE PER HMR) OF ESTIMATES					
		BEFORE HMR		AFTER HMR		DIFFERENCE*	
		COSTS ($)	QOL (QALY)	COSTS ($)	QOL (QALY)	COSTS ($)	QOL (QALY)
1	9, 13, 15, 21	26138.10 (435.64)	2.616 (0.044)	23407.52 (390.13)	2.526 (0.042)	-2730.58 (-45.51)	-0.090 (-0.001)
2	10, 14, 18, 22	54802.98 (913.38)	3.931 (0.066)	38984.38 (649.74)	2.641 (0.044)	-15818.59 (-263.64)	-1.290 (-0.022)
3	16, 19, 23	6792.25 (113.20)	0.198 (0.003)	5988.60 (99.81)	0.365 (0.006)	-803.65 (-13.39)	0.167 (0.003)
4	12, 17, 20, 24	28872.94 (481.22)	3.487 (0.058)	21561.29 (359.35)	2.469 (0.041)	-7311.64 (-121.86)	-1.018 (-0.017)

* Negative numbers denote savings or gained QOL

Unsurprisingly, Kruskal Wallis tests revealed that there were significant differences between the panels' raw estimates of both costs and QOL changes occurring as a result of the HMRs (for costs, $\chi^2(3,240)=61.3$, $P<0.001$; for QOL, $\chi^2(3,240)=68.8$, $P<0.001$).

It was concluded from these results that the plan to analyse a further 120 HMRs (30 HMRs unique to each panel) and combine these results with those of the 60 common HMRs would not be appropriate as the different panels did not evaluate the HMRs consistently. Consequently, the full economic analysis was undertaken using only the 60 HMRs assessed by every expert, as each expert's opinion could be considered to be of equivalent plausibility to that of the other experts only for these HMRs. The results of the panel's estimates of the remaining HMRs are presented in Section 6.3.4.2.

6.3.4 Health resource costs and quality of life

The methodology used to calculate the estimate of the costs and QOL changes resulting from the HMRs is complex and required multiple stepwise calculations. The methodology is explained in detail via a worked example in Appendix XXI. Briefly, the estimates were generated as follows:

1. for every DRP, each consequence selected by the experts and the experts' estimates of the before- and after- HMR probabilities for the three health states linked to the consequence were multiplied by the parameters in the consequences table (cost and QOL) that describe each health state;
2. these results were then summed to provide an overall estimate for each parameter for every DRP both before and after the HMR;
3. the potential drug cost changes resulting from the DRP were appended as an additional parameter for each DRP;
4. these before- and after- estimates of each parameter for each DRP were summed with the estimates for the remaining DRPs in the same HMR to generate estimates for each parameter both before and after the HMR;
5. the attribution estimates and whether or not the pharmacists' recommendations were implemented were applied where appropriate to the before- and after- HMR scenarios to generate final estimates for each parameter before and after the HMR.

Using this methodology, estimates of costs and QOL with and without the HMR were generated, allowing for comparisons to be made to investigate the clinical and cost-effectiveness of HMRs.

6.3.4.1 Dataset of 60 HMRs assessed by every expert

6.3.4.1.1 Clinical outcomes of HMRs

The clinical outcomes of the HMRs were expressed in terms of the estimated probability of the consequences they prevented and incurred. Table 114 shows the number of HMRs in which each consequence was predicted to occur, and the median of the probability estimates for the occurrence of each severity level of each consequence in the presence and absence of the HMR. The median of the differences in probabilities of each health state occurring between the with- and without-HMRs scenarios are also presented to illustrate the overall effect of the HMR on each health state; any health state where the median is greater than zero indicates that there were more HMRs in which the consequence was less likely to subsequently occur as a result of the HMR.

TABLE 114 - ESTIMATED CLINICAL OUTCOMES OF HMRS - MEDIAN OF ESTIMATES OF THE PERCENTAGE PROBABILITY OF CONSEQUENCES OCCURRING AT DIFFERENT SEVERITY LEVELS WITH AND WITHOUT THE HMR, AND THE NUMBER OF HMRS IN WHICH THESE CONSEQUENCES WERE PREDICTED TO OCCUR (BASELINE SCENARIO)

SEVERITY LEVEL	MILD				MODERATE				SEVERE			
CONSEQUENCE	NUMBER OF PATIENTS	MEDIAN (IQR) PROBABILITY (%) WITHOUT HMR	WITH HMR	DIFFERENCE*	NUMBER OF PATIENTS	MEDIAN (IQR) PROBABILITY (%) WITHOUT HMR	WITH HMR	DIFFERENCE*	NUMBER OF PATIENTS	MEDIAN (IQR) PROBABILITY (%) WITHOUT HMR	WITH HMR	DIFFERENCE*
Acidosis	16	4.02 (4.90)	3.61 (5.21)	0.00 (0.48)	16	1.51 (2.21)	1.44 (2.02)	0.00 (0.32)	16	0.57 (0.52)	0.49 (0.53)	0.00 (0.11)
Alkalosis	1	0.11	0.10	0.01	1	0.03	0.03	0.00	1	0.01	0.01	0.00
Allergic reaction	4	0.67 (2.68)	0.62 (2.64)	0.08 (0.13)	6	0.11 (0.35)	0.11 (0.25)	0.01 (0.11)	6	0.01 (0.15)	0.01 (0.09)	0.00 (0.06)
Anaemia	14	0.53 (2.61)	0.57 (2.35)	0.05 (0.17)	14	0.31 (0.79)	0.29 (0.76)	0.01 (0.08)	11	0.08 (0.32)	0.08 (0.30)	0.00 (0.04)
Anxiety	5	4.00 (3.75)	4.04 (3.84)	-0.01 (0.15)	5	2.31 (1.92)	2.31 (1.92)	-0.01 (0.02)	4	0.96 (1.13)	0.96 (1.13)	-0.01 (0.00)
Arrhythmia	18	4.67 (8.75)	4.52 (7.67)	0.04 (0.31)	18	1.95 (2.62)	1.85 (2.60)	0.03 (0.10)	17	0.35 (1.01)	0.34 (0.91)	0.01 (0.05)
Asthma	10	10.31 (10.67)	10.25 (10.99)	0.04 (0.35)	10	1.42 (2.69)	1.41 (2.70)	0.02 (0.11)	10	0.31 (0.34)	0.29 (0.33)	0.02 (0.04)
Bleeding, non-specific	14	4.13 (5.04)	4.09 (4.81)	0.08 (0.43)	14	0.96 (1.37)	0.98 (1.21)	0.03 (0.09)	14	0.36 (0.50)	0.35 (0.45)	0.01 (0.07)
Bone marrow suppression	3	0.16 (3.05)	0.15 (2.00)	0.01 (1.06)	3	0.12 (1.02)	0.11 (0.71)	0.01 (0.32)	3	0.05 (0.23)	0.04 (0.15)	0.01 (0.08)
Cerebrovascular event	20	1.64 (4.84)	1.67 (4.85)	-0.01 (0.09)	20	1.35 (3.04)	1.41 (3.05)	-0.01 (0.08)	19	0.81 (1.91)	0.86 (1.93)	-0.01 (0.04)
Chronic airways disease	11	6.92 (6.98)	6.41 (6.23)	0.42 (0.87)	11	2.34 (2.98)	2.20 (2.92)	0.14 (0.63)	9	0.50 (0.99)	0.50 (0.96)	0.01 (0.05)
CNS depression	8	1.56 (2.60)	1.45 (2.39)	-0.01 (0.19)	8	0.38 (0.87)	0.40 (0.57)	0.00 (0.04)	6	0.19 (0.28)	0.15 (0.27)	0.00 (0.03)
Confusion	25	4.79 (8.35)	4.64 (8.41)	0.05 (0.16)	25	1.93 (3.42)	1.91 (3.35)	0.01 (0.06)	23	0.45 (0.73)	0.44 (0.74)	0.01 (0.02)
Constipation	16	4.62 (16.67)	4.63 (16.49)	-0.03 (0.22)	17	1.43 (8.12)	1.42 (7.29)	-0.01 (0.21)	10	0.62 (1.57)	0.65 (1.59)	0.00 (0.07)
Dementia	3	2.56 (5.71)	2.82 (5.72)	0.01 (0.28)	3	0.56 (1.35)	0.67 (1.36)	0.00 (0.11)	0			
Depression	8	3.76 (4.91)	3.84 (4.73)	-0.03 (0.27)	8	2.56 (2.68)	2.60 (2.72)	-0.02 (0.08)	6	0.99 (2.32)	1.00 (2.52)	-0.01 (0.39)
Diarrhoea	12	1.23 (11.86)	1.28 (11.44)	0.09 (0.53)	12	0.46 (5.71)	0.44 (5.66)	0.01 (0.15)	11	0.11 (1.04)	0.10 (1.21)	0.01 (0.06)

Severity level	Mild				Moderate				Severe			
	Number of patients	Median (IQR) probability (%)			Number of patients	Median (IQR) probability (%)			Number of patients	Median (IQR) probability (%)		
Consequence		Without HMR	With HMR	Difference*		Without HMR	With HMR	Difference*		Without HMR	With HMR	Difference*
Gastrointestinal bleeding	24	1.79 (3.36)	1.78 (3.26)	0.02 (0.16)	24	0.80 (1.44)	0.78 (1.28)	0.01 (0.08)	22	0.43 (0.77)	0.35 (0.75)	0.01 (0.03)
Headache	1	1.33	1.31	0.03	1	0.33	0.32	0.01	1	0.03	0.03	0.00
Heart failure	10	3.87 (11.48)	3.88 (11.34)	-0.05 (0.31)	10	1.06 (8.56)	1.09 (8.51)	-0.06 (0.18)	10	0.33 (1.77)	0.33 (1.59)	-0.01 (0.16)
Hypercalcaemia	3	0.52 (1.33)	0.55 (1.17)	0.06 (0.24)	3	0.45 (0.49)	0.48 (0.41)	0.03 (0.14)	3	0.28 (0.23)	0.23 (0.25)	0.01 (0.07)
Diabetes	14	8.40 (9.06)	7.98 (9.10)	-0.03 (0.32)	14	3.44 (5.89)	3.55 (5.48)	-0.02 (0.15)	14	0.69 (1.29)	0.72 (1.20)	0.00 (0.05)
Hyperkalaemia	10	1.59 (6.98)	1.58 (6.54)	0.00 (0.28)	10	0.58 (2.61)	0.59 (2.48)	0.00 (0.10)	8	0.23 (0.70)	0.23 (0.67)	0.00 (0.05)
Hypertension	17	9.32 (17.43)	8.83 (18.04)	0.05 (1.00)	17	2.60 (9.60)	3.00 (10.54)	0.05 (0.71)	15	0.45 (1.29)	0.45 (1.35)	0.00 (0.07)
Hyperthyroidism	2	0.65	0.64	0.01	2	0.32	0.32	0.01	2	0.09	0.09	0.00
Hypocalcaemia	4	0.46 (0.52)	0.40 (0.47)	0.07 (0.08)	4	0.26 (0.37)	0.21 (0.34)	0.02 (0.09)	4	0.18 (0.17)	0.16 (0.12)	0.02 (0.06)
Hypoglycaemia	10	6.57 (8.54)	6.52 (8.23)	0.07 (0.38)	10	2.11 (3.59)	2.40 (3.44)	0.02 (0.12)	10	0.79 (1.38)	0.74 (1.31)	0.01 (0.09)
Hypokalaemia	11	1.43 (2.22)	1.43 (2.01)	0.03 (0.31)	12	0.54 (0.85)	0.52 (0.80)	0.01 (0.05)	6	0.14 (0.61)	0.13 (0.72)	0.00 (0.09)
Hypotension	16	1.29 (4.19)	1.23 (4.22)	0.02 (0.29)	17	0.76 (2.25)	0.69 (2.25)	0.01 (0.23)	14	0.25 (1.57)	0.23 (1.56)	0.00 (0.15)
Hypothyroidism	3	1.66 (7.01)	1.65 (6.10)	0.46	3	1.42 (3.16)	1.40 (2.78)	0.20	3	0.17 (0.33)	0.17 (0.29)	0.02
Infection, general	4	2.50 (6.49)	2.04 (5.57)	0.41 (1.12)	4	1.11 (4.74)	0.93 (4.28)	0.21 (0.49)	3	0.28 (0.41)	0.22 (0.45)	0.00 (0.11)
Insomnia	5	15.36 (15.00)	15.10 (14.09)	0.12 (0.98)	6	2.58 (14.52)	2.57 (13.90)	0.03 (0.59)	5	1.92 (10.62)	1.93 (10.00)	0.01 (0.62)
Liver disease	15	0.65 (2.38)	0.57 (2.62)	0.01 (0.08)	15	0.49 (0.85)	0.47 (1.01)	0.01 (0.05)	13	0.06 (0.42)	0.07 (0.35)	0.00 (0.04)
Myocardial ischaemia	26	2.87 (6.15)	2.92 (6.28)	-0.02 (0.11)	27	1.39 (3.79)	1.45 (3.69)	-0.01 (0.10)	26	0.69 (1.58)	0.71 (1.47)	0.00 (0.04)
Myopathy	10	5.70 (4.86)	4.96 (5.10)	0.18 (0.81)	10	2.40 (3.02)	1.90 (3.14)	0.08 (0.22)	8	0.91 (1.28)	0.77 (1.31)	0.05 (0.12)
Nausea	12	1.83 (5.07)	1.95 (4.84)	0.04 (0.65)	12	0.34 (1.07)	0.29 (1.14)	0.01 (0.17)	10	0.07 (0.17)	0.07 (0.20)	0.00 (0.05)

Severity level	Mild				Moderate				Severe			
Consequence	Number of patients	Median (IQR) probability (%) Without HMR	With HMR	Difference*	Number of patients	Median (IQR) probability (%) Without HMR	With HMR	Difference*	Number of patients	Median (IQR) probability (%) Without HMR	With HMR	Difference*
Oedema	11	2.45 (6.48)	2.55 (6.58)	0.02 (0.82)	11	0.71 (4.06)	0.71 (4.23)	0.01 (0.36)	9	0.14 (0.99)	0.13 (0.96)	0.01 (0.10)
Osteoporosis	19	6.21 (12.84)	5.82 (12.70)	0.06 (0.17)	20	2.73 (6.86)	2.48 (6.70)	0.08 (0.18)	19	0.45 (0.98)	0.45 (0.97)	0.00 (0.02)
Pain	29	4.62 (16.20)	4.62 (15.54)	0.00 (0.15)	28	2.12 (9.57)	2.34 (9.20)	0.00 (0.51)	25	0.53 (1.01)	0.49 (1.05)	0.00 (0.05)
Rash	6	0.82 (3.64)	0.73 (3.70)	0.05 (0.36)	6	0.39 (1.84)	0.34 (2.05)	0.02 (0.33)	6	0.11 (0.73)	0.10 (0.87)	0.01 (0.16)
Renal dysfunction	28	3.93 (9.00)	3.46 (7.99)	0.06 (0.65)	29	1.48 (3.88)	1.36 (3.64)	0.05 (0.29)	26	0.39 (1.69)	0.40 (1.70)	0.02 (0.05)
Respiratory depression	7	6.60 (5.71)	6.26 (5.71)	0.11 (0.51)	7	2.14 (2.44)	2.14 (2.24)	0.00 (0.30)	6	0.17 (1.92)	0.17 (1.91)	0.00 (0.02)
Seizures	1	3.28	3.13	0.15	1	2.33	2.21	0.12	1	0.52	0.49	0.03
Serotonin toxicity	4	2.71 (2.38)	2.92 (2.22)	-0.04 (0.51)	4	0.30 (0.24)	0.33 (0.20)	-0.02 (0.08)	4	0.04 (0.04)	0.05 (0.02)	-0.01 (0.02)
Urinary incontinence	1	4.40	4.18	0.22	1	1.70	1.63	0.07	1	0.13	0.11	0.01
Urinary retention	2	0.85	0.88	-0.03	2	0.41	0.43	-0.02	2	0.30	0.31	-0.01
Urinary tract infection	1	2.77	2.94	-0.16	1	1.35	1.51	-0.16	1	0.13	0.15	-0.02

*Negative numbers denote an increase in likelihood of the consequence occurring

The consequence most frequently affected by the HMRs was *Pain*, the probability of which was considered by the experts to be affected by the HMR in almost half of the patients (29, 48.3%). Somewhat surprisingly, there was a high frequency of changes in the probability of the consequence of *Confusion*, with the likelihood of this consequence being affected in 25 of the HMRs (41.7%). More predictably, the likelihood of other consequences occurring that were frequency selected by the experts included *Renal dysfunction* (28 patients, 46.7%), *Myocardial ischaemia* (26, 43.3%) and *Gastrointestinal bleeding* (24, 40%).

To assess whether the HMRs were likely to have resulted in significant overall benefits or detriments on each health state, Wilcoxon Signed Rank tests were used to compare the probabilities of the consequences occurring at the three severity levels in the presence and the absence of the HMRs. The results of this analysis are shown in Table 115.

TABLE 115 - ESTIMATED CLINICAL OUTCOMES OF HMRS - WILCOXON SIGNED RANK TEST RESULTS COMPARING MEDIAN OF ESTIMATES OF THE PERCENTAGE PROBABILITY OF CONSEQUENCES OCCURRING AT DIFFERENT SEVERITY LEVELS WITH AND WITHOUT THE HMR (BASELINE SCENARIO).

	SEVERITY LEVEL					
	MILD		MODERATE		SEVERE	
CONSEQUENCE	MEDIAN (IQR) OF DIFFERENCES	TEST RESULT*	MEDIAN (IQR) OF DIFFERENCES	TEST RESULT*	MEDIAN (IQR) OF DIFFERENCES	TEST RESULT*
Acidosis	0.00 (0.48)	*Z*=-0.663, *P*=0.508	0.00 (0.32)	*Z*=-0.524, *P*=0.600	0.00 (0.11)	*Z*=-0.454, *P*=0.650
Allergic reaction	0.08 (0.13)	*Z*=-1.069, *P*=0.285	0.01 (0.11)	*Z*=-1.153, *P*=0.249	0.00 (0.06)	***Z*=-1.992, *P*=0.046**
Anaemia	0.05 (0.17)	*Z*=-1.642, *P*=0.101	0.01 (0.08)	*Z*=-1.503, *P*=0.133	0.00 (0.04)	*Z*=-1.070, *P*=0.285
Anxiety	-0.01 (0.15)	*Z*=-0.365, *P*=0.715	-0.01 (0.02)	*Z*=-1.473, *P*=0.141	-0.01 (0.00)	*Z*=-1.604, *P*=0.109
Arrhythmia	0.04 (0.31)	***Z*=-2.112, *P*=0.035**	0.03 (0.10)	***Z*=-2.156, *P*=0.031**	0.01 (0.05)	***Z*=-2.722, *P*=0.006**
Asthma	0.04 (0.35)	*Z*=-1.599, *P*=0.110	0.02 (0.11)	*Z*=-1.481, *P*=0.139	0.02 (0.04)	*Z*=-2.073, *P*=0.038
Bleeding, non-specific	0.08 (0.43)	*Z*=-0.866, *P*=0.386	0.03 (0.09)	*Z*=-1.580, *P*=0.114	0.01 (0.07)	*Z*=-1.580, *P*=0.114
Bone marrow suppression	0.01 (1.06)	*Z*=-1.604, *P*=0.109	0.01 (0.32)	*Z*=-1.604, *P*=0.109	0.01 (0.08)	*Z*=-1.604, *P*=0.109
Cerebrovascular event	-0.01 (0.09)	*Z*=-0.734, *P*=0.463	-0.01 (0.08)	*Z*=-0.970, *P*=0.332	-0.01 (0.04)	*Z*=-1.138, *P*=0.255
Chronic airways disease	0.42 (0.87)	***Z*=-1.960, *P*=0.050**	0.14 (0.63)	*Z*=-1.599, *P*=0.110	0.01 (0.05)	*Z*=-1.153, *P*=0.249
CNS depression	-0.01 (0.19)	*Z*=-0.085, *P*=0.933	0.00 (0.04)	*Z*=-0.507, *P*=0.612	0.00 (0.03)	*Z*=-1.153, *P*=0.249
Confusion	0.05 (0.16)	***Z*=-3.036, *P*=0.002**	0.01 (0.06)	***Z*=-2.972, *P*=0.003**	0.01 (0.02)	***Z*=-2.173, *P*=0.030**
Constipation	-0.03 (0.22)	*Z*=-1.136, *P*=0.256	-0.01 (0.21)	*Z*=-0.621, *P*=0.535	0.00 (0.07)	*Z*=-0.140, *P*=0.889
Depression	-0.03 (0.27)	*Z*=-0.700, *P*=0.484	-0.02 (0.08)	*Z*=-1.521, *P*=0.128	-0.01 (0.39)	*Z*=-1.753, *P*=0.080
Diabetes	-0.03 (0.32)	*Z*=-1.922, *P*=0.055	-0.02 (0.15)	*Z*=-1.503, *P*=0.133	0.00 (0.05)	*Z*=-1.569, *P*=0.117
Diarrhoea	0.09 (0.53)	*Z*=-1.580, *P*=0.114	0.01 (0.15)	*Z*=-0.764, *P*=0.445	0.01 (0.06)	*Z*=-1.125, *P*=0.260
Gastrointestinal bleeding	0.02 (0.16)	*Z*=-1.938, *P*=0.053	0.01 (0.08)	*Z*=-1.502, *P*=0.133	0.01 (0.03)	*Z*=-1.448, *P*=0.148

	Severity level					
	Mild		Moderate		Severe	
Consequence	Median (IQR) of differences	Test result*	Median (IQR) of differences	Test result*	Median (IQR) of differences	Test result*
Heart failure	-0.05 (0.31)	*Z*=-1.352, *P*=0.176	-0.06 (0.18)	*Z*=-1.540, *P*=0.123	-0.01 (0.16)	*Z*=-0.420, *P*=0.674
Hypercalcaemia	0.06 (0.24)	*Z*=-1.069, *P*=0.285	0.03 (0.14)	*Z*=-0.535, *P*=0.593	0.01 (0.07)	*Z*=-1.069, *P*=0.285
Hyperkalaemia	0.00 (0.28)	*Z*=-0.415, *P*=0.678	0.00 (0.10)	*Z*=-0.652, *P*=0.515	0.00 (0.05)	*Z*=-0.169, *P*=0.866
Hypertension	0.05 (1.00)	*Z*=-0.175, *P*=0.861	0.05 (0.71)	*Z*=-0.105, *P*=0.917	0.00 (0.07)	*Z*=-0.031, *P*=0.975
Hyperthyroidism	0.01	*Z*=-1.000, *P*=0.317	0.01	*Z*=-1.000, *P*=0.317	0.00	*Z*=-1.000, *P*=0.317
Hypocalcaemia	0.07 (0.08)	*Z*=-1.604, *P*=0.109	0.02 (0.09)	*Z*=-1.604, *P*=0.109	0.02 (0.06)	*Z*=-1.604, *P*=0.109
Hypoglycaemia	0.07 (0.38)	*Z*=-0.980, *P*=0.327	0.02 (0.12)	*Z*=-0.560, *P*=0.575	0.01 (0.09)	*Z*=-0.700, *P*=0.484
Hypokalaemia	0.03 (0.31)	*Z*=-0.357, *P*=0.721	0.01 (0.05)	*Z*=-0.445, *P*=0.657	0.00 (0.09)	*Z*=-0.524, *P*=0.600
Hypotension	0.02 (0.29)	*Z*=-0.284, *P*=0.776	0.01 (0.23)	*Z*=-0.170, *P*=0.865	0.00 (0.15)	*Z*=-0.471, *P*=0.638
Hypothyroidism	0.46	*Z*=-1.342, *P*=0.180	0.20	*Z*=-1.342, *P*=0.180	0.02	*Z*=-1.342, *P*=0.180
Infection, general	0.41 (1.12)	*Z*=-1.095, *P*=0.273	0.21 (0.49)	*Z*=-1.095, *P*=0.273	0.00 (0.11)	*Z*=-0.535, *P*=0.593
Insomnia	0.12 (0.98)	*Z*=-1.214, *P*=0.225	0.03 (0.59)	*Z*=-1.153, *P*=0.249	0.01 (0.62)	*Z*=-0.674, *P*=0.500
Liver disease	0.01 (0.08)	*Z*=-1.477, *P*=0.140	0.01 (0.05)	*Z*=-1.136, *P*=0.256	0.00 (0.04)	*Z*=-1.922, *P*=0.055
Myocardial ischaemia	-0.02 (0.11)	*Z*=-0.276, *P*=0.783	-0.01 (0.10)	*Z*=-0.639, *P*=0.523	0.00 (0.04)	*Z*=-0.669, *P*=0.503
Myopathy	0.18 (0.81)	***Z*=-2.191, *P*=0.028**	0.08 (0.22)	***Z*=-2.090, *P*=0.037**	0.05 (0.12)	***Z*=-2.100, *P*=0.036**
Nausea	0.04 (0.65)	*Z*=-0.866, *P*=0.386	0.01 (0.17)	*Z*=-0.866, *P*=0.386	0.00 (0.05)	*Z*=-0.280, *P*=0.779
Oedema	0.02 (0.82)	*Z*=-0.652, *P*=0.515	0.01 (0.36)	*Z*=-0.770, *P*=0.441	0.01 (0.10)	*Z*=-1.183, *P*=0.237
Osteoporosis	0.06 (0.17)	***Z*=-2.482, *P*=0.013**	0.08 (0.18)	***Z*=-2.635, *P*=0.008**	0.00 (0.02)	*Z*=-1.655, *P*=0.098
Pain	0.00 (0.15)	*Z*=-0.547, *P*=0.584	0.00 (0.51)	*Z*=-0.336, *P*=0.737	0.00 (0.05)	*Z*=-0.686, *P*=0.492

	Severity level					
	Mild		Moderate		Severe	
Consequence	Median (IQR) of differences	Test result*	Median (IQR) of differences	Test result*	Median (IQR) of differences	Test result*
Rash	0.05 (0.36)	*Z*=-0.943, *P*=0.345	0.02 (0.33)	*Z*=-0.943, *P*=0.345	0.01 (0.16)	*Z*=-0.943, *P*=0.345
Renal dysfunction	0.06 (0.65)	*Z*=-1.531, *P*=0.126	0.05 (0.29)	*Z*=-1.755, *P*=0.079	0.02 (0.05)	***Z*=-2.091, *P*=0.037**
Respiratory depression	0.11 (0.51)	*Z*=-0.730, *P*=0.465	0.00 (0.30)	*Z*=-0.405, *P*=0.686	0.00 (0.02)	*Z*=0.000, *P*=1.000
Serotonin toxicity	-0.04 (0.51)	*Z*=-0.365, *P*=0.715	-0.02 (0.08)	*Z*=-0.730, *P*=0.465	-0.01 (0.02)	*Z*=-0.730, *P*=0.465
Urinary retention	-0.03	*Z*=-1.342, *P*=0.180	-0.02	*Z*=-1.342, *P*=0.180	-0.01	*Z*=-1.342, *P*=0.180

*Wilcoxon Signed Rank test

Significant differences between the with- and without- HMR estimates were observed in several of the consequences, indicating that the HMRs potentially reduced the risk of each of these consequences occurring. Significant reductions in the likelihood of *Arrhythmias*, *Confusion* and *Myopathy* were observed at all severity levels ($P<0.05$). Furthermore, the estimated probability of the severe health states of *Allergic reaction*, *Asthma* and *Renal dysfunction* were also significantly lower in the with-HMR estimates compared to those without-HMRs, as were the mild and moderate health states for *Osteoporosis*.

However, as shown in Table 115, the absolute reduction in estimated risk resulting from the HMRs was minor for every consequence. As a result, the predicted effects of the HMRs on costs and QOL were limited, as presented in the following section.

6.3.4.1.2 Estimated cost and QOL effects of HMRs

The drug cost data, cost of the HMR, uptake data and the experts' predictions of attribution, the likely consequences and their probabilities were used to generate estimates of the costs and QOL occurring in the presence and absence of the HMRs, according to the methodology outlined in Appendix XXI. The estimated costs and QOL occurring without and with the HMRs for each patient are shown in Table 163 and Table 164 (Appendix XXII), respectively. As per the economic protocol, the estimates are for a 12-month period.

A summary of the overall costs and QOL effects occurring with and without the HMRs is presented in Table 116. On average, it was estimated that HMRs resulted in a gross saving of $85.79 per HMR, primarily resulting from reduced hospitalisation costs ($33.09, 38.6% of savings) and drug costs ($26.09, 30.5% of savings). However, this was insufficient to offset the cost of the HMR, and the average additional net cost of a HMR was $238.01 per patient compared to usual care. The HMRs were predicted to result in a minor improvement in QOL of an average of 0.001 QALYs per patient compared to usual care.

Wilcoxon Signed Rank tests were undertaken to compare the costs and QOL with and without HMRs. The results of these investigations are shown in Table 116. Notably, the HMRs were estimated to result in a significant increase in QOL and reductions in

every cost except for drug costs. However, as the magnitude of the estimated savings was small in most HMRs, the HMRs resulted in a significantly increased net cost compared to the no-HMR scenario.

TABLE 116 - AVERAGE PER PATIENT CHANGES IN COSTS AND QOL RESULTING FROM 60 COMMON HMRS - BASELINE SCENARIO

PARAMETER	WITHOUT HMR	WITH HMR	DIFFERENCE *	TEST RESULT†
Days of ill health	8.0	7.2	0.9	*Z*=-5.455, *P*<0.001
Disability incurred (QALY)	0.013	0.011	0.001	*Z*=-5.057, *P*<0.001
Annual drug costs ($)	3 405.52	3 379.43	26.09	*Z*=-1.814, *P*=0.070
Number of GP visits	5.9	5.4	0.5	*Z*=-6.110, *P*<0.001
Cost of GP visits ($)	171.20	155.87	15.33	*Z*=-6.235, *P*<0.001
Number of specialist visits	0.4	0.3	0.0	*Z*=-5.160, *P*<0.001
Cost of specialist visits ($)	21.34	18.97	2.37	*Z*=-5.426, *P*<0.001
Cost of investigations ($)	79.81	70.91	8.91	*Z*=-6.581, *P*<0.001
Days hospitalised	0.3	0.3	0.0	*Z*=-4.483, *P*<0.001
Cost of hospitalisation ($)	316.07	282.97	33.09	*Z*=-4.616, *P*<0.001
Cost of HMR ($)	0.00	323.80	-323.80	-
TOTAL COSTS ($)	3 993.95	4 231.95	-238.01	*Z*=6.383, *P*<0.001

* Negative numbers indicate increased cost †Wilcoxon Signed Rank tests

6.3.4.1.3 Differences between HMRs

The results of the economic modelling indicated that only four (6.7%) of the HMRs would have resulted in overall savings to the health system (that is, the savings were greater than the cost of the HMR). Nine of the HMRs (15%) were predicted to increase costs above that of the cost of the HMR; hence, it was estimated that most (85%) of the HMRs would have reduced costs, but not enough to offset the cost of providing the HMR. The cumulative costs and QOL effects of the HMRs are shown in Figure 43. The influence of the small numbers of HMRs that offset costs is apparent.

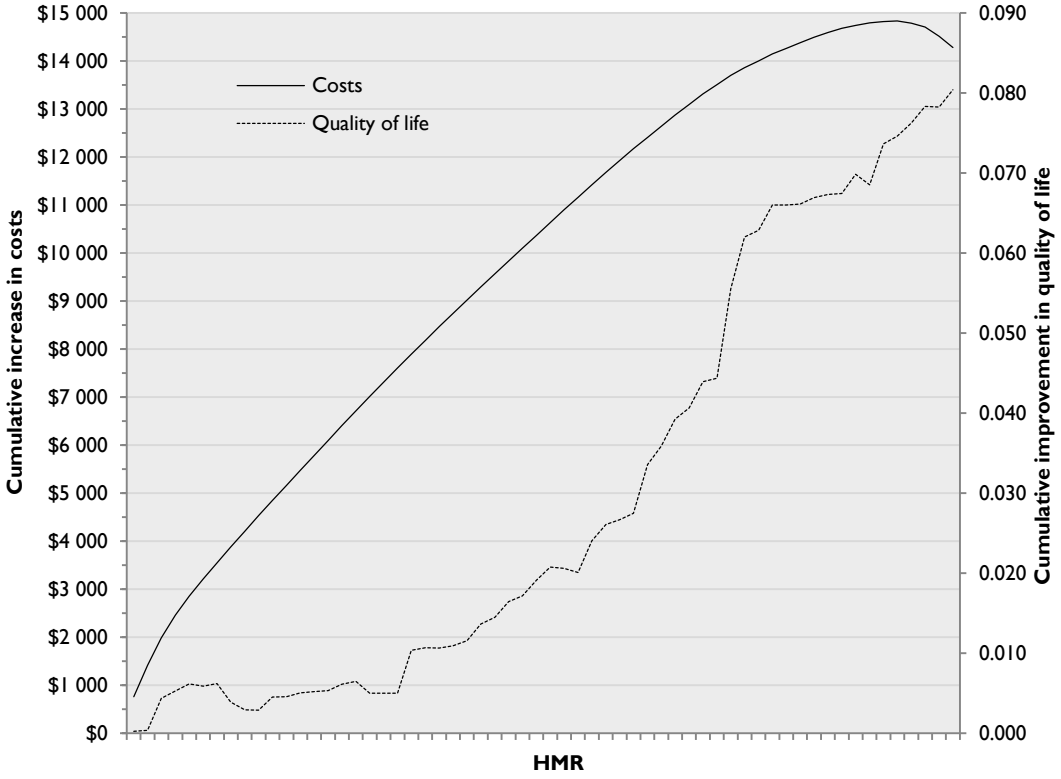

FIGURE 43 - CUMULATIVE EFFECTS OF HMRS ON COSTS AND QUALITY OF LIFE. NEGATIVE VALUES INDICATE SAVINGS OR REDUCED QOL.

It was somewhat concerning that the model predicted that 12 HMRs (20%) would have worsened patient QOL, one of which was a HMRs that completely offset costs. However, for these HMRs where it was predicted that QOL would have decreased, the magnitude of the decrease was generally minimal - in nine of the HMRs the change was less than 0.0001 QALYs per patient, and the remaining three HMRs were 0.0013, 0.0015 and 0.0023 QALYs per patient.

6.3.4.1.4 Cost and QOL effects of different DRP types

As the experts assessed individual DRPs (as opposed to overall HMRs), it was possible to investigate whether there were differences between DRP types in terms of the estimated outcomes of resolving the DRPs (that is, the costs and QOL effects). Table 166 and Table 167 (Appendix XXII) show the summed costs and QOL for each type and subtype of DRP that were estimated to have occurred, with and without the HMR.

Several differences were evident between the proportions of the DRP types and the effect of resolving them on costs and QOL. This is illustrated in Figure 44. DRPs classed as *Untreated indications* appeared to result in proportionally greater benefits on QOL than other types of DRPs. *Drug selection* DRPs appeared to result in proportionally greater savings than DRPs of most other DRP types. Conversely, the savings and QOL benefits of *Toxicity of adverse reaction* DRPs appeared to be proportionally less than the frequency of this DRP type.

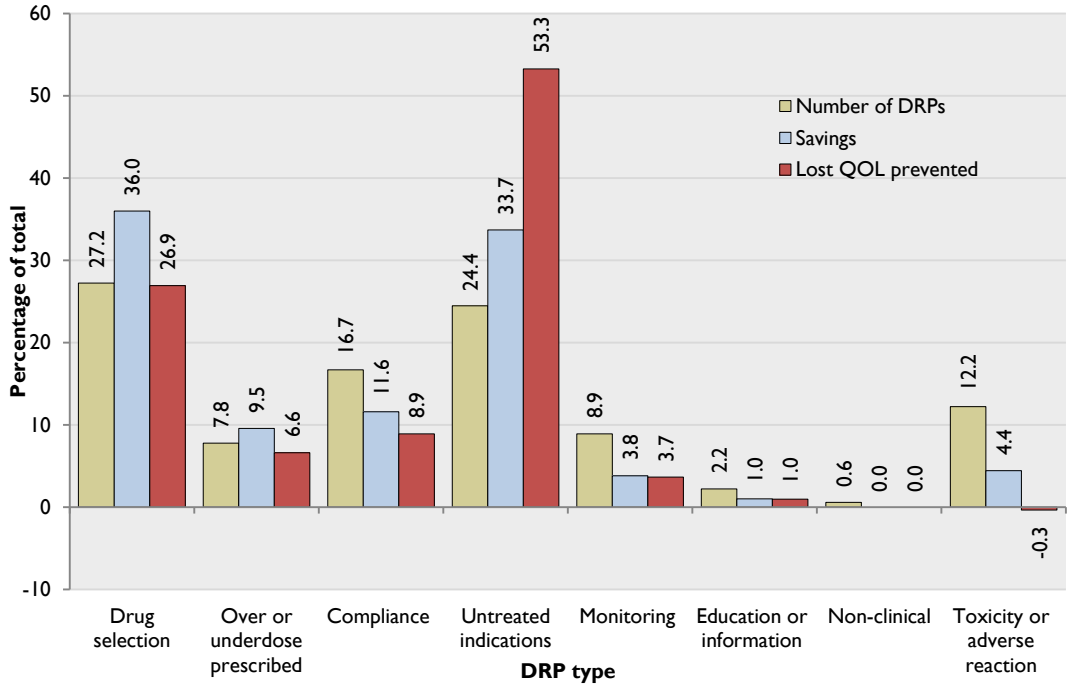

FIGURE 44 - DIFFERENCES IN PROPORTIONS OF TOTAL DRPS, SAVINGS AND QOL IN DATASET OF 60 HMRS ASSESSED BY EVERY EXPERT

6.3.4.1.5 Extrapolation to HMRs Australia-wide

To provide an indication of the cost and QOL outcomes of HMRs Australia-wide, the results of the analysis of the 60 common HMRs were extrapolated to the number of HMRs performed in Australia during the study period. MBS claim statistics were used to identify the number of HMRs that were undertaken in 2008 (equivalent data for pharmacies is not readily available).[21] From 1 January to 31 December 2008, GPs were reimbursed for 40 105 HMRs. Multiplication of this figure by the average savings and

QOL effects shown in Table 116 resulted in estimated outcomes of the HMR program Australia-wide in the subsequent 12-months shown in Table 117.

TABLE 117 - ESTIMATED OUTCOMES OF HMRS AUSTRALIA-WIDE IN 2008-09 EXTRAPOLATED FROM RESULTS OF THE VALMER STUDY

PARAMETER	TOTAL (40 105 HMRS)*
Days of ill health	34 471
Disability prevented (QALY)	54
Annual drug costs ($)	1 046 411
Number of GP visits	20 286
Cost of GP visits ($)	614 761
Number of specialist visits	1 559
Cost of specialist visits ($)	95 123
Cost of laboratory/pathology investigations ($)	357 197
Days hospitalised	1 277
Cost of hospitalisation ($)	1 327 225
Cost of HMR ($)	-12 985 999
TOTAL COSTS ($)	-9 545 282

* Negative numbers indicate increased cost

However, as discussed in Section 6.3.1, no DRPs were documented in 18 of the 661 HMRs (2.7%) in the VALMER study, and these HMRs were excluded from the economic analysis. As costs were still incurred in providing these HMRs, a more appropriate extrapolation of the results to the HMR program Australia-wide would appear to require inclusion of these HMRs in the calculation. The results of this extrapolation are shown in Table 118.

TABLE 118 - ESTIMATED OUTCOMES OF HMRS AUSTRALIA-WIDE IN 2008-09 EXTRAPOLATED FROM RESULTS OF THE VALMER STUDY (RECALCULATED USING EXCLUDED HMR DATA)

PARAMETER	NO DRPS IDENTIFIED IN HMR	DRPS IDENTIFIED IN HMR	TOTAL*
Number of HMRs	1092	39 013	40 105
Days of ill health	0	33 532	33 532
Disability prevented (QALY)	0	52	52
Annual drug costs ($)	0	1 017 919	1 017 919
Number of GP visits	0	19 733	19 733
Cost of GP visits ($)	0	598 022	598 022
Number of specialist visits	0	1 516	1 516
Cost of specialist visits ($)	0	92 533	92 533
Cost of laboratory/pathology investigations ($)	0	347 471	347 471
Days hospitalised	0	1 242	1 242
Cost of hospitalisation ($)	0	1 291 086	1 291 086
Cost of HMR ($)	-353 590	-12 632 409	-12 985 999
TOTAL COSTS ($)	**-353 590**	**-9 285 378**	**-9 638 968**

* Negative numbers indicate increased cost

The results of the VALMER study therefore indicated that in 2008-09, HMRs resulted in savings of approximately $3.3 million to the healthcare system and a QOL gain of 52 QALYs. However, these figures must be interpreted within the confines of the assumptions and limitations of the study, as discussed in Section 2.4.4 and Section 7.3.2, respectively.

6.3.4.2 Dataset of panel-specific HMRs

6.3.4.2.1 Patient characteristics and DRPs identified

In addition to the 60 HMRs assessed by every expert, a further 120 HMRs were assessed, whereby each expert was assigned to one of four panels and each panel assessed 30 HMRs unique that that panel. The lack of reliability between the panels in their assessment of the 60 common HMRs resulted in the assessment of the additional 120 HMRs being analysed separately; these results are presented in this section.

A summary of the general characteristics of the panel-specific patients is shown in Table 119.

TABLE 119 - CHARACTERISTICS OF PANEL-SPECIFIC PATIENTS

CHARACTERISTIC (MEAN ± SD UNLESS STATED OTHERWISE)	PANEL ONE (N=30)	TWO (N=30)	THREE (N=30)	FOUR (N=30)	OVERALL (N=120)
Number (%) of males	19 (63.3)	11 (36.7)	10 (33.3)	15 (50.0)	55 (45.8)
Age (years)	75.6 ± 11.9	78.0 ± 7.4	78.0 ± 10.0	78.4 ± 9.3	77.5 ± 9.7
Number of medical conditions	8.7 ± 3.7	10.5 ± 7.0	9.8 ± 6.0	9.1 ± 5.6	9.5 ± 5.7
Number of total medications	13.9 ± 3.9	13.6 ± 4.7	10.0 ± 3.6	11.9 ± 5.2	12.4 ± 4.6
Number of regular medications	11.4 ± 3.4	11.2 ± 3.8	8.2 ± 3.0	10.0 ± 3.7	10.2 ± 3.7
Median (IQR) monthly cost to PBS of regular medications ($)	154.02 (120.95)	203.60 (126.76)	144.71 (152.04)	173.30 (130.95)	174.19 (123.83)
Number of DRPs identified per HMR	3.7 ± 3.0	4.0 ± 1.7	3.6 ± 1.2	3.8 ± 1.3	3.8 ± 1.6

The types and subtypes of DRPs addressed in these HMRs are shown in Table 120. Of these 454 DRPs, the experts estimated the outcomes for 322 of them (70.9%).

TABLE 120 - FREQUENCY OF TYPES AND SUBTYPES OF DRPS IDENTIFIED IN DATASET OF 120 PANEL-SPECIFIC HMRS

DRP TYPE / SUBTYPE	PANEL ONE (N=30)	TWO (N=30)	THREE (N=30)	FOUR (N=30)	TOTAL
Drug selection	**22 (4.8)**	**31 (6.8)**	**26 (5.7)**	**29 (6.4)**	**108 (23.8)**
Duplication	1 (0.2)	3 (0.7)	4 (0.9)	1 (0.2)	9 (2.0)
Drug interaction	6 (1.3)	7 (1.5)	10 (2.2)	7 (1.5)	30 (6.6)
Wrong dosage form	(0.0)	1 (0.2)	(0.0)	1 (0.2)	2 (0.4)
Unnecessary therapy/no apparent current indication	6 (1.3)	8 (1.8)	5 (1.1)	11 (2.4)	30 (6.6)
Contraindications apparent	9 (2.0)	12 (2.6)	6 (1.3)	9 (2.0)	36 (7.9)
Other drug selection problem	(0.0)	(0.0)	1 (0.2)	(0.0)	1 (0.2)
Over or underdose prescribed	**5 (1.1)**	**14 (3.1)**	**9 (2.0)**	**10 (2.2)**	**38 (8.4)**
Dose too high	3 (0.7)	7 (1.5)	4 (0.9)	7 (1.5)	21 (4.6)
Dose too low	1 (0.2)	5 (1.1)	2 (0.4)	3 (0.7)	11 (2.4)
Other dose problem	1 (0.2)	2 (0.4)	3 (0.7)	(0.0)	6 (1.3)
Compliance	**12 (2.6)**	**12 (2.6)**	**14 (3.1)**	**20 (4.4)**	**58 (12.8)**
Taking too little	6 (1.3)	6 (1.3)	5 (1.1)	8 (1.8)	25 (5.5)
Taking too much	(0.0)	1 (0.2)	1 (0.2)	(0.0)	2 (0.4)
Difficulty using dosage form	3 (0.7)	(0.0)	2 (0.4)	1 (0.2)	6 (1.3)
Patient using out of date medication	(0.0)	2 (0.4)	(0.0)	1 (0.2)	3 (0.7)
Other compliance problem	3 (0.7)	3 (0.7)	6 (1.3)	10 (2.2)	22 (4.8)

DRP Type / Subtype	Panel				Total
	One (n=30)	Two (n=30)	Three (n=30)	Four (n=30)	
Untreated indications	44 (9.7)	32 (7.0)	29 (6.4)	29 (6.4)	134 (29.5)
Condition not adequately treated	**27 (5.9)**	**21 (4.6)**	**16 (3.5)**	**17 (3.7)**	**81 (17.8)**
Therapy required	15 (3.3)	11 (2.4)	13 (2.9)	12 (2.6)	51 (11.2)
Other untreated indication problem	2 (0.4)	(0.0)	(0.0)	(0.0)	2 (0.4)
Monitoring	**8 (1.8)**	**7 (1.5)**	**18 (4.0)**	**8 (1.8)**	**41 (9.0)**
Laboratory monitoring	7 (1.5)	7 (1.5)	16 (3.5)	7 (1.5)	37 (8.1)
Non-laboratory monitoring	1 (0.2)	(0.0)	2 (0.4)	1 (0.2)	4 (0.9)
Education or information	**1 (0.2)**	**3 (0.7)**	**1 (0.2)**	**2 (0.4)**	**7 (1.5)**
Patient drug information request	(0.0)	(0.0)	(0.0)	(0.0)	0 (0.0)
Confusion about therapy	(0.0)	1 (0.2)	(0.0)	(0.0)	1 (0.2)
Demonstration of device	1 (0.2)	1 (0.2)	(0.0)	(0.0)	2 (0.4)
Disease management or advice	(0.0)	1 (0.2)	1 (0.2)	(0.0)	2 (0.4)
Other education or information problem	(0.0)	(0.0)	(0.0)	2 (0.4)	2 (0.4)
Non-clinical	**1 (0.2)**	**2 (0.4)**	**2 (0.4)**	**5 (1.1)**	**10 (2.2)**
Weight management problem	(0.0)	(0.0)	1 (0.2)	(0.0)	1 (0.2)
Dietary problem	(0.0)	(0.0)	(0.0)	2 (0.4)	2 (0.4)
Smoking problem	(0.0)	(0.0)	(0.0)	2 (0.4)	2 (0.4)
Alcohol problem	(0.0)	1 (0.2)	1 (0.2)	(0.0)	2 (0.4)
Other non-clinical problem	1 (0.2)	1 (0.2)	(0.0)	1 (0.2)	3 (0.7)
Toxicity or adverse reaction	**19 (4.2)**	**19 (4.2)**	**9 (2.0)**	**11 (2.4)**	**58 (12.8)**
Toxicity caused by dose	2 (0.4)	6 (1.3)	(0.0)	2 (0.4)	10 (2.2)
Toxicity caused by drug interaction	4 (0.9)	(0.0)	(0.0)	(0.0)	4 (0.9)
Toxicity evident	13 (2.9)	13 (2.9)	9 (2.0)	9 (2.0)	44 (9.7)
Other toxicity/adverse effect problem	(0.0)	(0.0)	(0.0)	(0.0)	0 (0.0)
Total	**112 (24.7)**	**120 (26.4)**	**108 (23.8)**	**114 (25.1)**	**454 (100.0)**

6.3.4.2.2 Clinical outcomes of HMRs

To estimate the clinical outcomes of these HMRs, they were assessed by the experts using the same methodology employed in the assessment of the 60 common HMRs (Section 6.3.4.1.1). The clinical outcomes of the HMRs were expressed in terms of the estimated probability of the consequences they prevented and incurred. The number of HMRs in which each consequence was predicted to occur and the median of the probability estimates for the occurrence of each severity level of each consequence, in the presence and absence of the HMR, are shown in Table 121.

TABLE 121 - ESTIMATED CLINICAL OUTCOMES OF HMRS - MEDIAN OF ESTIMATES OF THE PERCENTAGE PROBABILITY OF CONSEQUENCES OCCURRING AT DIFFERENT SEVERITY LEVELS WITH AND WITHOUT THE HMR, AND THE NUMBER OF HMRS IN WHICH THESE CONSEQUENCES WERE PREDICTED TO OCCUR (BASELINE SCENARIO, PANEL SPECIFIC HMRS)

SEVERITY LEVEL	MILD				MODERATE				SEVERE			
CONSEQUENCE	NUMBER (%) OF PATIENTS	MEDIAN (IQR) PROBABILITY (%) WITHOUT HMR	WITH HMR	DIFFERENCE*	NUMBER (%) OF PATIENTS	MEDIAN (IQR) PROBABILITY (%) WITHOUT HMR	WITH HMR	DIFFERENCE*	NUMBER (%) OF PATIENTS	MEDIAN (IQR) PROBABILITY (%) WITHOUT HMR	WITH HMR	DIFFERENCE*
Acidosis	8 (6.7)	7.94 (13.22)	8.25 (12.48)	0.14 (1.21)	8 (6.7)	6.03 (14.84)	6.09 (14.41)	0.00 (0.84)	8 (6.7)	1.17 (13.01)	1.31 (12.47)	0.00 (0.62)
Alkalosis	2 (1.7)	15.57	14.74	0.83	2 (1.7)	15.57	14.74	0.83	2 (1.7)	15.57	14.74	0.83
Allergic reaction	5 (4.2)	0.70 (7.63)	0.66 (7.69)	0.00 (0.09)	5 (4.2)	0.50 (0.93)	0.50 (0.95)	0.00 (0.05)	5 (4.2)	0.11 (0.21)	0.09 (0.20)	0.00 (0.02)
Anaemia	9 (7.5)	2.57 (5.87)	2.43 (5.74)	0.12 (0.27)	9 (7.5)	0.88 (1.37)	0.68 (1.09)	0.02 (0.16)	9 (7.5)	0.00 (0.20)	0.00 (0.15)	0.00 (0.05)
Anxiety	2 (1.7)	15.66	15.82	-0.15	2 (1.7)	2.95	2.99	-0.05	2 (1.7)	0.73	0.74	0.00
Arrhythmia	16 (13.3)	5.37 (8.80)	5.26 (9.76)	0.02 (0.93)	16 (13.3)	1.99 (2.57)	1.77 (3.12)	0.02 (0.20)	16 (13.3)	0.64 (0.53)	0.61 (0.64)	0.00 (0.09)
Asthma	8 (6.7)	6.17 (6.81)	5.99 (7.77)	0.00 (0.35)	8 (6.7)	2.37 (1.79)	2.47 (1.64)	0.00 (0.12)	8 (6.7)	0.54 (0.64)	0.54 (0.66)	0.00 (0.03)
Bleeding, non-specific	22 (18.3)	4.38 (11.73)	4.62 (11.46)	0.00 (0.55)	22 (18.3)	1.45 (3.49)	1.80 (3.71)	0.00 (0.19)	22 (18.3)	0.44 (0.92)	0.43 (0.97)	0.00 (0.06)
Bone marrow suppression	1 (0.8)	11.25	11.25	0.00	1 (0.8)	0.75	0.75	0.00	1 (0.8)	0.04	0.04	0.00
Cerebrovascular event	23 (19.2)	2.67 (7.87)	2.67 (7.07)	0.00 (0.34)	23 (19.2)	1.53 (3.74)	1.50 (3.53)	0.00 (0.20)	23 (19.2)	0.68 (1.49)	0.70 (1.72)	0.00 (0.26)
Chronic Airways Disease	13 (10.8)	12.69 (19.02)	12.64 (19.65)	0.00 (0.70)	13 (10.8)	5.58 (21.74)	5.25 (21.84)	0.00 (0.26)	13 (10.8)	1.52 (2.91)	1.48 (3.34)	0.00 (0.02)
CNS Depression	8 (6.7)	5.04 (16.81)	5.31 (17.08)	-0.09 (2.80)	8 (6.7)	0.89 (7.86)	0.95 (8.34)	-0.03 (0.34)	8 (6.7)	0.21 (1.81)	0.17 (1.89)	0.00 (0.09)
Confusion	22 (18.3)	8.03 (13.79)	7.94 (14.80)	0.00 (0.94)	22 (18.3)	1.95 (4.31)	2.57 (4.28)	0.00 (0.32)	22 (18.3)	0.98 (1.34)	0.94 (1.37)	0.00 (0.20)
Constipation	18 (15.0)	18.66 (28.68)	18.59 (27.72)	0.21 (1.15)	18 (15.0)	4.08 (14.00)	3.92 (14.72)	0.06 (0.49)	18 (15.0)	0.44 (1.69)	0.35 (1.81)	0.00 (0.10)
Dementia	2 (1.7)	10.47	9.94	0.53	2 (1.7)	2.08	2.08	0.00	2 (1.7)	0.29	0.29	0.00
Depression	7 (5.8)	7.89 (15.12)	6.80 (16.97)	0.00 (1.37)	7 (5.8)	3.82 (7.95)	3.39 (8.84)	0.00 (1.20)	7 (5.8)	0.60 (1.35)	0.57 (1.34)	0.00 (0.06)
Diarrhoea	9 (7.5)	3.42 (14.33)	2.83 (17.58)	-0.50 (2.54)	9 (7.5)	1.23 (5.28)	1.44 (6.46)	-0.20 (1.07)	9 (7.5)	0.44 (1.00)	0.56 (1.12)	-0.10 (0.12)

Severity level	Mild				Moderate				Severe			
	Number (%) of patients	Median (IQR) probability (%)			Number (%) of patients	Median (IQR) probability (%)			Number (%) of patients	Median (IQR) probability (%)		
Consequence		Without HMR	With HMR	Difference*		Without HMR	With HMR	Difference*		Without HMR	With HMR	Difference*
Gastrointestinal bleeding	25 (20.8)	3.00 (3.63)	2.92 (3.81)	0.00 (0.34)	25 (20.8)	1.38 (1.50)	1.37 (1.75)	0.00 (0.18)	25 (20.8)	0.56 (0.85)	0.57 (0.90)	0.00 (0.11)
Glaucoma	1 (0.8)	7.75	7.75	0.00	1 (0.8)	4.75	4.75	0.00	1 (0.8)	0.25	0.25	0.00
Headache	4 (3.3)	2.97 (7.16)	2.65 (7.13)	0.01 (0.59)	4 (3.3)	0.48 (2.32)	0.40 (2.33)	0.00 (0.17)	4 (3.3)	0.00 (0.26)	0.00 (0.27)	0.00 (0.00)
Heart Failure	18 (15.0)	5.66 (13.04)	5.60 (12.68)	0.04 (0.64)	18 (15.0)	2.74 (7.86)	2.50 (10.37)	0.02 (0.37)	18 (15.0)	0.75 (1.97)	0.68 (1.99)	0.01 (0.08)
Hypercalcaemia	2 (1.7)	4.85	5.48	-0.63	2 (1.7)	1.63	1.88	-0.25	2 (1.7)	0.03	0.04	-0.01
Diabetes	8 (6.7)	18.80 (37.90)	16.48 (35.79)	0.38 (3.00)	8 (6.7)	4.44 (7.80)	4.74 (6.42)	0.21 (0.91)	8 (6.7)	0.90 (2.07)	0.73 (2.01)	0.00 (0.19)
Hyperkalaemia	10 (8.3)	12.18 (26.18)	9.99 (26.57)	0.00 (1.93)	10 (8.3)	3.92 (14.50)	5.83 (7.69)	0.00 (1.15)	10 (8.3)	0.71 (3.51)	0.71 (1.82)	0.00 (0.22)
Hypertension	18 (15.0)	7.08 (20.76)	7.08 (21.79)	0.00 (0.15)	18 (15.0)	6.21 (15.89)	5.43 (17.08)	0.00 (0.13)	18 (15.0)	0.41 (1.63)	0.42 (1.63)	0.00 (0.00)
Hyperthyroidism	1 (0.8)	2.33	1.33	1.00	1 (0.8)	0.00	0.00	0.00	1 (0.8)	0.00	0.00	0.00
Hypocalcaemia	1 (0.8)	2.09	1.66	0.43	1 (0.8)	1.09	0.91	0.17	1 (0.8)	0.21	0.17	0.04
Hypoglycaemia	6 (5.0)	7.81 (19.73)	6.56 (17.58)	0.66 (2.69)	6 (5.0)	4.27 (15.17)	3.16 (18.57)	0.17 (5.27)	6 (5.0)	0.71 (2.30)	0.79 (1.97)	0.00 (0.23)
Hypokalaemia	9 (7.5)	3.24 (5.91)	3.70 (6.88)	0.00 (0.50)	9 (7.5)	0.38 (2.08)	0.41 (1.02)	0.00 (1.15)	9 (7.5)	0.00 (0.46)	0.00 (0.42)	0.00 (0.04)
Hypotension	25 (20.8)	5.00 (11.98)	5.00 (10.48)	0.00 (0.69)	25 (20.8)	1.38 (3.99)	1.51 (3.34)	0.00 (0.38)	25 (20.8)	0.17 (0.74)	0.24 (0.81)	0.00 (0.08)
Hypothyroidism	3 (2.5)	2.33 (6.04)	1.33 (5.17)	0.87 (1.00)	3 (2.5)	1.32 (12.78)	1.19 (3.89)	0.13 (8.89)	3 (2.5)	0.00 (0.22)	0.00 (0.18)	0.00 (0.04)
Infection, general	5 (4.2)	1.66 (7.79)	1.74 (8.02)	-0.11 (0.84)	5 (4.2)	0.96 (2.00)	0.97 (2.42)	-0.06 (0.45)	5 (4.2)	0.18 (0.16)	0.19 (0.19)	-0.01 (0.03)
Insomnia	5 (4.2)	5.89 (13.44)	5.78 (13.56)	0.00 (0.43)	5 (4.2)	2.60 (16.30)	2.65 (10.88)	0.04 (5.52)	5 (4.2)	0.29 (1.22)	0.31 (1.24)	0.00 (0.04)
Liver disease	3 (2.5)	0.98 (1.02)	0.58 (0.52)	0.41 (0.51)	3 (2.5)	0.21 (0.23)	0.21 (0.11)	0.07 (0.19)	3 (2.5)	0.05 (0.10)	0.05 (0.07)	0.00 (0.05)
Myocardial ischaemia	39 (32.5)	5.00 (10.14)	3.86 (10.80)	0.00 (0.24)	39 (32.5)	1.90 (3.13)	2.46 (3.14)	0.00 (0.11)	39 (32.5)	1.00 (1.36)	0.92 (1.37)	0.00 (0.02)
Myopathy	11 (9.2)	4.39 (9.46)	3.57 (9.77)	0.00 (0.41)	11 (9.2)	2.27 (5.23)	1.04 (5.67)	0.00 (0.27)	11 (9.2)	0.35 (3.28)	0.34 (3.73)	0.00 (0.10)

Severity level	Mild				Moderate				Severe			
	Number (%) of patients	Median (IQR) probability (%)			Number (%) of patients	Median (IQR) probability (%)			Number (%) of patients	Median (IQR) probability (%)		
Consequence		Without HMR	With HMR	Difference*		Without HMR	With HMR	Difference*		Without HMR	With HMR	Difference*
Nausea	7 (5.8)	2.19 (1.32)	2.31 (1.87)	0.07 (0.38)	7 (5.8)	1.15 (1.07)	1.16 (1.31)	0.04 (0.24)	7 (5.8)	0.17 (0.28)	0.13 (0.41)	0.00 (0.09)
Oedema	10 (8.3)	7.50 (18.59)	7.50 (17.50)	-0.02 (3.65)	10 (8.3)	2.57 (0.93)	2.60 (0.81)	0.00 (1.05)	10 (8.3)	0.48 (0.79)	0.40 (0.50)	0.00 (0.01)
Osteoporosis	19 (15.8)	6.25 (24.71)	5.71 (24.61)	0.00 (0.61)	19 (15.8)	3.16 (3.98)	2.50 (4.06)	0.00 (0.27)	19 (15.8)	0.28 (1.44)	0.28 (1.35)	0.00 (0.03)
Pain	40 (33.3)	9.62 (21.20)	11.44 (21.22)	-0.01 (1.05)	40 (33.3)	3.28 (11.05)	3.99 (11.24)	0.00 (0.50)	40 (33.3)	0.44 (2.05)	0.53 (2.11)	0.00 (0.09)
Parkinsonism	3 (2.5)	2.93 (12.27)	3.94 (13.40)	-1.01 (1.13)	3 (2.5)	0.94 (8.63)	1.11 (9.43)	-0.17 (0.81)	3 (2.5)	0.00 (5.31)	0.00 (5.80)	0.00 (0.49)
Psychosis	1 (0.8)	5.72	6.78	-1.06	1 (0.8)	0.89	1.11	-0.21	1 (0.8)	0.41	0.46	-0.05
Rash	6 (5.0)	25.07 (29.22)	20.93 (28.48)	0.59 (2.53)	6 (5.0)	1.74 (6.10)	1.43 (5.97)	0.06 (0.31)	6 (5.0)	0.18 (1.21)	0.18 (0.98)	0.00 (0.08)
Renal dysfunction	23 (19.2)	4.33 (19.89)	4.83 (21.38)	0.00 (0.38)	23 (19.2)	3.00 (8.67)	3.00 (7.00)	0.00 (0.25)	23 (19.2)	0.92 (2.40)	1.17 (2.63)	0.00 (0.07)
Respiratory depression	2 (1.7)	2.97	2.86	0.11	2 (1.7)	0.62	0.55	0.07	2 (1.7)	0.13	0.12	0.01
Serotonin toxicity	3 (2.5)	0.87 (18.13)	1.10 (19.38)	-0.23 (1.25)	3 (2.5)	0.87 (1.81)	1.10 (1.94)	-0.12 (0.23)	3 (2.5)	0.00 (0.35)	0.00 (0.44)	0.00 (0.09)
Urinary incontinence	4 (3.3)	3.50 (24.17)	4.00 (23.44)	0.00 (1.73)	4 (3.3)	3.15 (13.02)	2.94 (14.60)	-0.10 (2.22)	4 (3.3)	0.15 (0.42)	0.14 (0.47)	0.00 (0.06)
Urinary retention	3 (2.5)	2.30 (1.89)	2.08 (1.67)	0.01 (0.64)	3 (2.5)	1.25 (1.31)	1.16 (1.22)	0.00 (0.25)	3 (2.5)	0.46 (1.09)	0.48 (0.65)	0.00 (0.45)
Urinary tract infection	1 (0.8)	1.62	1.58	0.04	1 (0.8)	0.65	0.63	0.01	1 (0.8)	0.16	0.15	0.01

*Negative numbers denote an increase in likelihood of the consequence occurring

The consequences that were frequently selected by the experts in these HMRs were not substantially different to those seen for the 60 common HMRs (Table 114), with *Pain*, *Myocardial ischaemia* and *Gastrointestinal bleeding* again being the most frequently chosen. However, the mean number of unique consequences selected for each patient in these HMRs was less than that for the panel specific reviews (8.4 versus 4.2 consequences per HMR, $t(178)=9.44$, $P<0.001$). This was presumably due to the smaller numbers of experts who assessed these HMRs, given the broad spread of consequences selected and minimal agreement between the experts observed in the initial analysis (Section 6.3.3.2).

As per the analysis for the 60 common HMRs, Wilcoxon Signed Rank tests were used to compare the probabilities of the consequences occurring at the three severity levels in the presence and the absence of the HMRs. The results of this analysis are shown in Table 122.

TABLE 122 - ESTIMATED CLINICAL OUTCOMES OF HMRS - WILCOXON SIGNED RANK TEST RESULTS COMPARING MEDIAN OF ESTIMATES OF THE PERCENTAGE PROBABILITY OF CONSEQUENCES OCCURRING AT DIFFERENT SEVERITY LEVELS WITH AND WITHOUT THE HMR (PANEL SPECIFIC HMRS, BASELINE SCENARIO).

	SEVERITY LEVEL					
	MILD		MODERATE		SEVERE	
CONSEQUENCE	MEDIAN (IQR) OF DIFFERENCES	TEST RESULT	MEDIAN (IQR) OF DIFFERENCES	TEST RESULT	MEDIAN (IQR) OF DIFFERENCES	TEST RESULT
Acidosis	0.14 (1.21)	*Z*=-0.338, *P*=0.735	0.00 (0.84)	*Z*=-0.524, *P*=0.600	0.00 (0.62)	*Z*=-1.153, *P*=0.249
Allergic reaction	0.00 (0.09)	*Z*=-1.342, *P*=0.180	0.00 (0.05)	*Z*=-1.604, *P*=0.109	0.00 (0.02)	*Z*=-1.461, *P*=0.144
Anaemia	0.12 (0.27)	*Z*=-1.540, *P*=0.123	0.02 (0.16)	*Z*=-1.680, *P*=0.093	0.00 (0.05)	*Z*=-1.826, *P*=0.068
Anxiety	-0.15	*Z*=-1.000, *P*=0.317	-0.05	*Z*=-1.000, *P*=0.317	0	*Z*=-1.000, *P*=0.317
Arrhythmia	0.02 (0.93)	*Z*=-0.879, *P*=0.379	0.02 (0.20)	*Z*=-0.398, *P*=0.691	0.00 (0.09)	*Z*=-0.157, *P*=0.875
Asthma	0.00 (0.35)	*Z*=-0.105, *P*=0.917	0.00 (0.12)	*Z*=-0.674, *P*=0.500	0.00 (0.03)	*Z*=-0.405, *P*=0.686
Bleeding, non-specific	0.00 (0.55)	*Z*=-0.022, *P*=0.983	0.00 (0.19)	*Z*=-0.065, *P*=0.948	0.00 (0.06)	*Z*=-0.196, *P*=0.845
Cerebrovascular event	0.00 (0.34)	*Z*=-0.734, *P*=0.463	0.00 (0.20)	*Z*=-0.784, *P*=0.433	0.00 (0.26)	*Z*=-1.285, *P*=0.199
Chronic airways disease	0.00 (0.70)	*Z*=-0.561, *P*=0.575	0.00 (0.26)	*Z*=-0.840, *P*=0.401	0.00 (0.02)	*Z*=-0.338, *P*=0.735
CNS depression	-0.09 (2.80)	*Z*=-0.280, *P*=0.779	-0.03 (0.34)	*Z*=-0.338, *P*=0.735	0.00 (0.09)	*Z*=-0.365, *P*=0.715
Confusion	0.00 (0.94)	*Z*=-0.632, *P*=0.528	0.00 (0.32)	*Z*=-0.040, *P*=0.968	0.00 (0.20)	*Z*=-0.454, *P*=0.650
Constipation	0.21 (1.15)	*Z*=-0.879, *P*=0.379	0.06 (0.49)	*Z*=-0.931, *P*=0.352	0.00 (0.10)	*Z*=-0.459, *P*=0.646
Depression	0.00 (1.37)	*Z*=-0.105, *P*=0.917	0.00 (1.20)	*Z*=-0.314, *P*=0.753	0.00 (0.06)	*Z*=-0.314, *P*=0.753
Diabetes	0.38 (3.00)	*Z*=-1.183, *P*=0.237	0.21 (0.91)	*Z*=-1.183, *P*=0.237	0.00 (0.19)	*Z*=-0.676, *P*=0.499
Diarrhoea	-0.50 (2.54)	*Z*=-1.400, *P*=0.161	-0.20 (1.07)	*Z*=-1.680, *P*=0.093	-0.10 (0.12)	***Z*=-2.032, *P*=0.042**
Heart failure	0.04 (0.64)	*Z*=-1.778, *P*=0.075	0.02 (0.37)	*Z*=-1.255, *P*=0.209	0.01 (0.08)	*Z*=-1.956, *P*=0.050

	Severity level					
	Mild		Moderate		Severe	
Consequence	Median (IQR) of differences	Test result	Median (IQR) of differences	Test result	Median (IQR) of differences	Test result
Hypercalcaemia	-0.63	*Z*=-1.000, *P*=0.317	-0.25	*Z*=-1.000, *P*=0.317	-0.01	*Z*=-1.000, *P*=0.317
Hyperkalaemia	0.00 (1.93)	*Z*=0.000, *P*=1.000	0.00 (1.15)	*Z*=-0.280, *P*=0.779	0.00 (0.22)	*Z*=-0.734, *P*=0.463
Hypertension	0.00 (0.15)	*Z*=-0.059, *P*=0.953	0.00 (0.13)	*Z*=-0.445, *P*=0.657	0.00 (0.00)	*Z*=0.000, *P*=1.000
Hypoglycaemia	0.66 (2.69)	*Z*=-1.214, *P*=0.225	0.17 (5.27)	*Z*=-0.314, *P*=0.753	0.00 (0.23)	*Z*=-0.365, *P*=0.715
Hypokalaemia	0.00 (0.50)	*Z*=-0.736, *P*=0.462	0.00 (1.15)	*Z*=-1.214, *P*=0.225	0.00 (0.04)	*Z*=-1.342, *P*=0.180
Hypotension	0.00 (0.69)	*Z*=-1.167, *P*=0.243	0.00 (0.38)	*Z*=-0.845, *P*=0.398	0.00 (0.08)	*Z*=-1.758, *P*=0.079
Hypothyroidism	0.87 (1.00)	*Z*=-1.342, *P*=0.180	0.13 (8.89)	*Z*=-1.342, *P*=0.180	0.00 (0.04)	*Z*=-1.000, *P*=0.317
Infection, general	-0.11 (0.84)	*Z*=-0.944, *P*=0.345	-0.06 (0.45)	*Z*=-0.730, *P*=0.465	-0.01 (0.03)	*Z*=-1.095, *P*=0.273
Insomnia	0.00 (0.43)	*Z*=-0.730, *P*=0.465	0.04 (5.52)	*Z*=-0.674, *P*=0.500	0.00 (0.04)	*Z*=-0.535, *P*=0.593
Liver disease	0.41 (0.51)	*Z*=-1.069, *P*=0.285	0.07 (0.19)	*Z*=-1.069, *P*=0.285	0.00 (0.05)	*Z*=-0.535, *P*=0.593
Myocardial ischaemia	0.00 (0.24)	*Z*=-0.068, *P*=0.946	0.00 (0.11)	*Z*=-1.410, *P*=0.159	0.00 (0.02)	*Z*=-0.081, *P*=0.936
Myopathy	0.00 (0.41)	*Z*=-0.357, *P*=0.721	0.00 (0.27)	*Z*=-0.178, *P*=0.859	0.00 (0.10)	*Z*=-0.845, *P*=0.398
Nausea	0.07 (0.38)	*Z*=-0.676, *P*=0.499	0.04 (0.24)	*Z*=0.000, *P*=1.000	0.00 (0.09)	*Z*=-0.730, *P*=0.465
Oedema	-0.02 (3.65)	*Z*=-1.183, *P*=0.237	0.00 (1.05)	*Z*=-1.183, *P*=0.237	0.00 (0.01)	*Z*=-0.674, *P*=0.500
Osteoporosis	0.00 (0.61)	*Z*=-1.572, *P*=0.116	0.00 (0.27)	*Z*=-0.568, *P*=0.570	0.00 (0.03)	*Z*=-0.035, *P*=0.972
Pain	-0.01 (1.05)	***Z*=-2.410, *P*=0.016**	0.00 (0.50)	***Z*=-2.417, *P*=0.016**	0.00 (0.09)	***Z*=-2.776, *P*=0.006**
Rash	0.59 (2.53)	***Z*=-2.023, *P*=0.043**	0.06 (0.31)	*Z*=-1.826, *P*=0.068	0.00 (0.08)	*Z*=-1.604, *P*=0.109
Renal dysfunction	0.00 (0.38)	*Z*=-1.287, *P*=0.198	0.00 (0.25)	*Z*=-0.672, *P*=0.501	0.00 (0.07)	*Z*=-1.241, *P*=0.215

	Severity level					
	Mild		Moderate		Severe	
Consequence	Median (IQR) of differences	Test result	Median (IQR) of differences	Test result	Median (IQR) of differences	Test result
Respiratory depression	0.11	*Z*=-1.000, *P*=0.317	0.07	*Z*=-1.000, *P*=0.317	0.01	*Z*=-1.000, *P*=0.317
Serotonin toxicity	-0.23 (1.25)	*Z*=-1.342, *P*=0.180	-0.12 (0.23)	*Z*=-1.342, *P*=0.180	0.00 (0.09)	*Z*=-1.000, *P*=0.317
Urinary retention	0.01 (0.64)	*Z*=-0.535, *P*=0.593	0.00 (0.25)	*Z*=-0.535, *P*=0.593	0.00 (0.45)	*Z*=-0.535, *P*=0.593

In these HMRs, the experts estimated that the HMRs would result in significant reductions in the likelihood of *Mild* and *Severe Heart failure*, and *Mild Rash*. In contrast to the results for the 60 common HMRs, in which there was no consequence that had an increased probability of occurring because of the HMR, an increased probability of *Severe Diarrhoea* was estimated to occur in the panel-specific HMRs. Furthermore, the results for the consequence of *Pain* were somewhat contradictory, in that an increased probability due to the HMRs was observed at the *Mild* severity level, whereas the with-HMR probabilities were minimally but significantly lower at the higher severity levels.

6.3.4.2.3 Estimated cost and QOL effects of HMRs

Estimates of the cost and QOL changes occurring in the presence and absence of the HMRs were generated using drug cost data, cost of the HMR, uptake data and the experts' predictions of attribution, the likely consequences and their probabilities. The estimated costs and QOL occurring without and with the HMRs, for each patient are shown in Table 168 and Table 169 (Appendix XXII), and a summary of these data is presented in Table 123.

TABLE 123 - AVERAGE PER PATIENT CHANGES IN COSTS AND QOL RESULTING FROM 120 PANEL-SPECIFIC HMRS - BASELINE SCENARIO

PARAMETER	WITHOUT HMR	WITH HMR	DIFFERENCE *	TEST RESULT†
Days of ill health	7.3	6.7	0.6	*Z*=-5.393, *P*<0.001
Disability incurred (QALY)	0.012	0.012	0.000	*Z*=-4.004, *P*<0.001
Annual drug costs ($)	2 407.87	2 401.76	6.11	*Z*=-0.864, *P*=0.387
Number of GP visits	5.2	4.8	0.4	*Z*=-5.834, *P*<0.001
Cost of GP visits ($)	145.60	132.29	13.31	*Z*=-5.647, *P*<0.001
Number of specialist visits	0.3	0.3	0.0	*Z*=-4.987, *P*<0.001
Cost of specialist visits ($)	20.24	17.86	2.38	*Z*=-4.972, *P*<0.001
Cost of investigations ($)	68.70	62.74	5.96	*Z*=-5.625, *P*<0.001
Days hospitalised	0.3	0.3	0.0	*Z*=-3.566, *P*<0.001
Cost of hospitalisation ($)	303.73	281.66	22.07	*Z*=-3.418, *P*=0.001
Cost of HMR ($)	0.00	0.00	0.00	-
TOTAL COSTS ($)	2 946.14	3 220.11	-273.97	*Z*=-8.957, *P*<0.001

* Negative numbers indicate increased cost †Wilcoxon Signed Rank tests

As observed with the 60 common HMRs, the 120 panel-specific HMRs were estimated to result in improvements in QOL and significant savings for each parameter except for drug costs. The magnitude of the total savings resulting from the HMRs was lower than that observed with the common HMRs, with the average gross saving being $49.83 per HMR. Consequently, the estimated average additional cost of a HMR was $273.97 per patient compared to usual care. Furthermore, the difference in QOL was negligible, with the difference between the with- and without-HMR estimates being an average of 0.0004 QALYs per patient.

There were substantial differences between the panels with regards to their estimates of the costs and QOL effects of the panel-specific HMRs. Summary statistics for the parameter estimates for each panel are shown in Table 124. Of particular note are the results for Panel 4, in which it was estimated that the HMRs were likely to result in an overall slight loss of QOL and increased healthcare service utilisation costs compared to usual care. The HMRs assessed by the remaining panels were predicted to improve QOL and reduce costs, although the magnitude of these improvements was again small.

TABLE 124 - PREDICTED COSTS AND QOL CHANGES RESULTING FROM 120 PANEL-SPECIFIC HMRS

PARAMETER			REVIEW PANEL (N=30 FOR EACH)*			
			1	2	3	4
Costs ($)	Healthcare service utilisation (GP and specialist visits, hospitalisation and laboratory/ pathology)	Total	1113.10	2500.77	1674.90	-41.21
		Average per HMR	37.10	83.36	55.83	-1.37
		Median	24.79	65.46	-0.47	31.88
		Range	-122.90 to 230.45	-56.01 to 457.71	-557.02 to 1983.15	-1 087.53 to 238.19
	Drugs	Total	866.34	310.65	1 216.09	-1 660.53
		Average per HMR	28.88	10.36	40.54	-55.35
		Median	0.00	0.00	0.00	0.00
		Range	-65.77 to 242.98	-231.40 to 529.38	-191.56 to 480.34	-1734.79 to 299.81
	Total (incl. HMR)	Total	-7 734.56	-6 902.57	-6 823.01	-11 415.74
		Average per HMR	-257.82	-230.09	-227.43	-380.52
		Median	-300.86	-258.34	-323.80	-304.60
		Range	-492.59 to 81.27	-381.74 to 149.57	-880.82 to 1 883.26	-2024.71 to -15.36
QOL (QALY)		Total	0.026	0.083	0.004	-0.013
		Average per HMR	0.001	0.003	0.000	0.000
		Median	0.000	0.001	0.000	0.000
		Range	-0.004 to 0.005	-0.004 to 0.035	-0.014 to 0.008	-0.021 to 0.005

* Negative numbers indicate increased cost or lost QOL

6.4 Cost-utility and scenario analysis - dataset of 60 HMRs assessed by every expert

6.4.1 Overview

For the 60 HMRs that were assessed by every expert, it was estimated that the HMRs would improve QOL slightly (an average of 0.001 QALYs per patient), but not offset costs compared to usual care (an averaged increased cost of $238.01 per patient). A cost-utility analysis was therefore undertaken to investigate the cost-effectiveness of the HMRs. A number of assumptions were made in the baseline analysis (discussed in Section 2.4.4); therefore, a sensitivity analysis was conducted for changes in the following variables:

1. HMR cost; increased by 10%, or decreased to the amount paid only to the pharmacy.
2. attribution component; 100% of the potential benefits and detriments resulting from the HMRs assigned to the medication review.
3. proportion of the pharmacists' recommendations that were implemented following the HMR; implementation of recommendations increased to 100%, then decreased to 42% (the lowest rate of implemented recommendations reported in previous studies of HMRs).[126]
4. DRPs not assessed by the experts added to the model; each DRP not included in the expert assessment was valued at the average value of the assessed DRPs, discounted by 0%, 25%, 50% and 75%.

For each scenario, thresholds of $50 000 and $150 000 per QALY gained are included to indicate cost-effectiveness according to WHO definitions of *highly cost-effective* and *cost-effective*, respectively.[185]

6.4.2 Baseline scenario

The baseline scenario estimates of the total and average per patient changes in costs and QOL resulting from the HMRs are shown in Table 125, with the ICER being $177 566 per QALY gained.

TABLE 125 - AVERAGE PER PATIENT CHANGES IN COSTS AND QOL RESULTING FROM 60 COMMON HMRS - BASELINE SCENARIO

PARAMETER	WITHOUT HMR	WITH HMR	DIFFERENCE *	TEST RESULT†
Days of ill health	8.0	7.2	0.9	*Z*=-5.455, *P*<0.001
Disability incurred (QALY)	0.013	0.011	0.001	*Z*=-5.057, *P*<0.001
Annual drug costs ($)	3 405.52	3 379.43	26.09	*Z*=-1.814, *P*=0.070
Number of GP visits	5.9	5.4	0.5	*Z*=-6.110, *P*<0.001
Cost of GP visits ($)	171.20	155.87	15.33	*Z*=-6.235, *P*<0.001
Number of specialist visits	0.4	0.3	0.0	*Z*=-5.160, *P*<0.001
Cost of specialist visits ($)	21.34	18.97	2.37	*Z*=-5.426, *P*<0.001
Cost of investigations ($)	79.81	70.91	8.91	*Z*=-6.581, *P*<0.001
Days hospitalised	0.3	0.3	0.0	*Z*=-4.483, *P*<0.001
Cost of hospitalisation ($)	316.07	282.97	33.09	*Z*=-4.616, *P*<0.001
Cost of HMR ($)	0.00	323.80	-323.80	-
TOTAL COSTS ($)	3 993.95	4 231.95	-238.01	*Z*=6.383, *P*<0.001

* Negative numbers indicate increased cost †Wilcoxon Signed Rank tests

Figure 45 shows the ICERs for the 5000 resamples of the baseline scenario data.

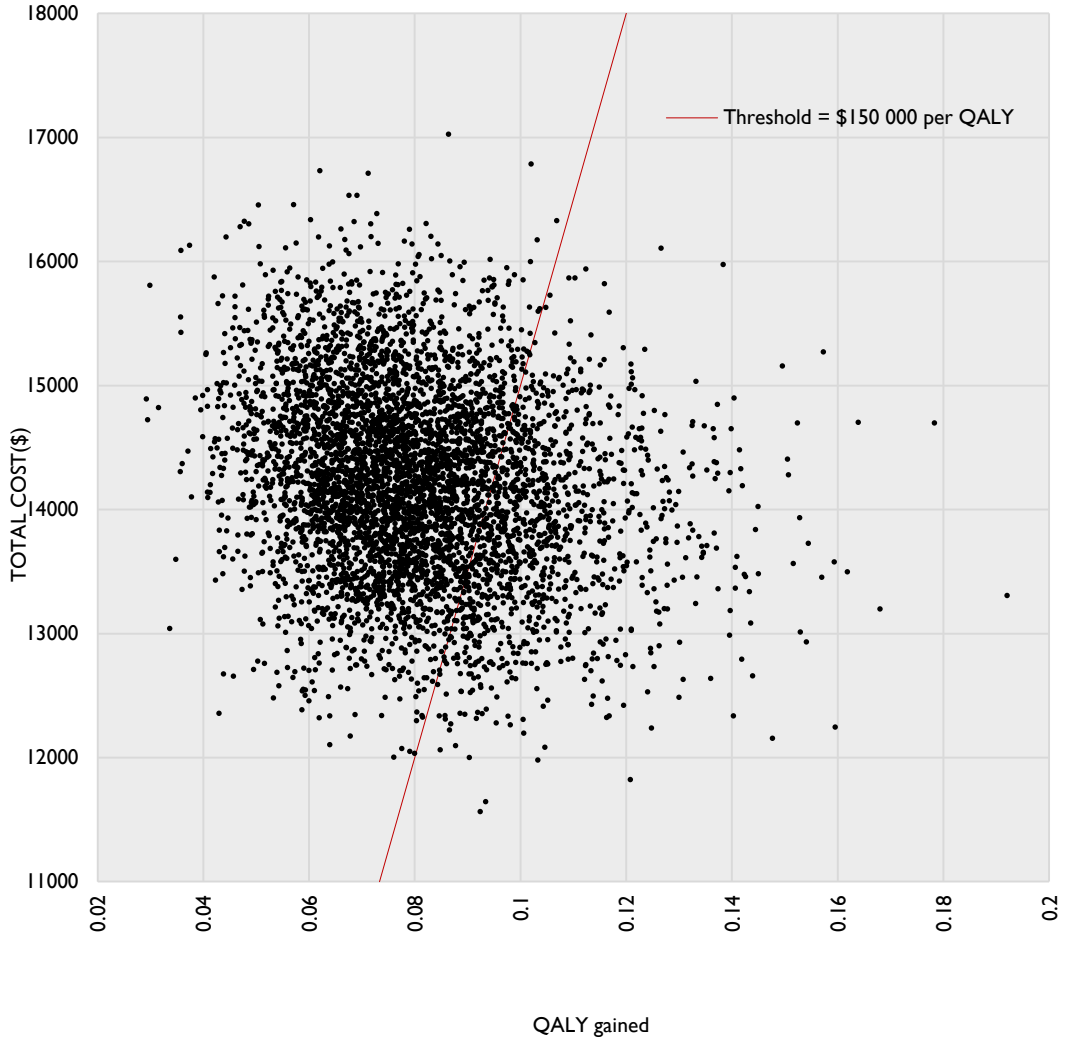

FIGURE 45 - RESAMPLED INCREMENTAL COST-EFFECTIVENESS RATIOS FOR HMRS VERSUS USUAL CARE: BASELINE SCENARIO

The CEAC generated using this data is shown in Figure 46. At a threshold of $50 000 per QALY gained, the baseline analysis had a 0% probability of being highly cost-effective. At a threshold of $150 000 per QALY gained, the probability of cost-effectiveness was 22.2%.

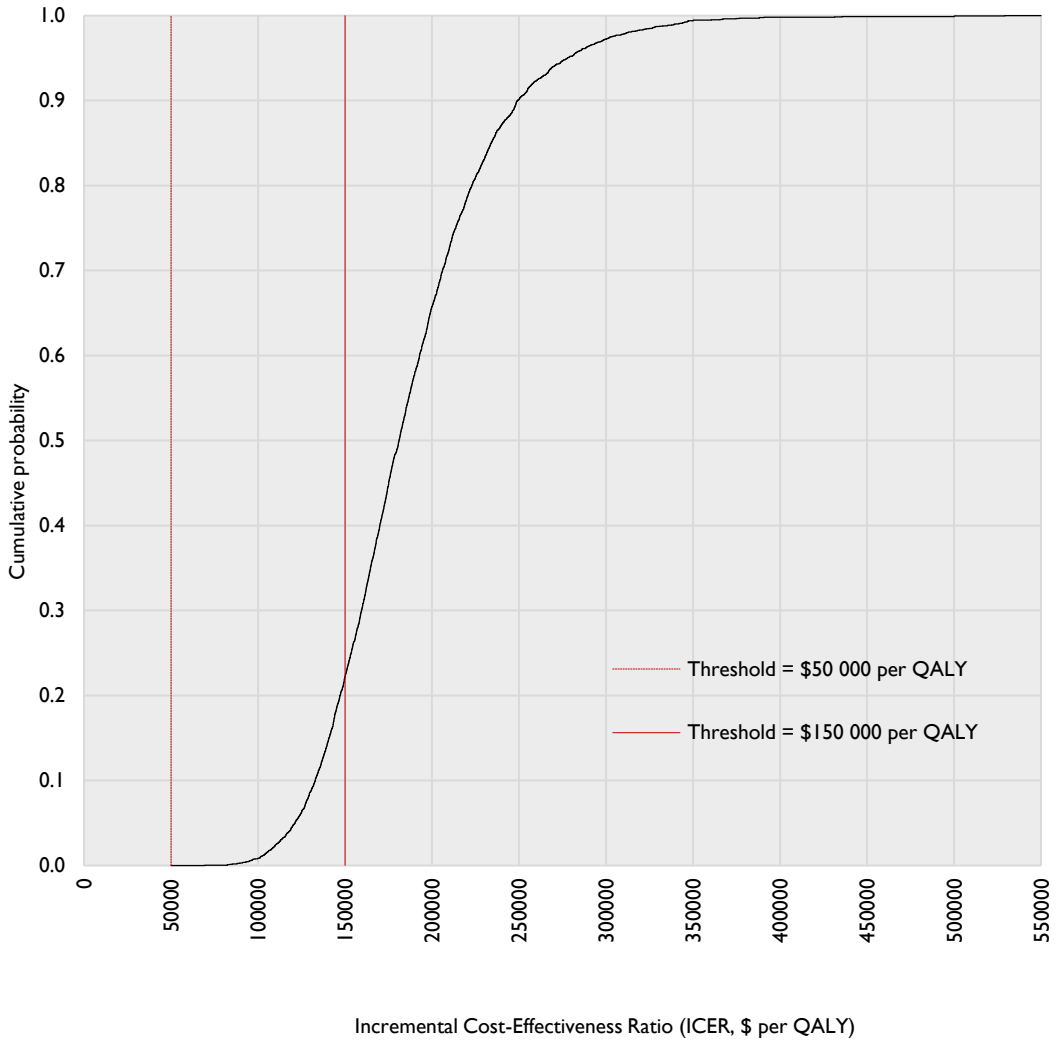

FIGURE 46 - COST-EFFECTIVENESS ACCEPTABILITY CURVE, GENERATED USING RESAMPLED DATA, FOR BASELINE SCENARIO

6.4.3 HMR cost

6.4.3.1 Accounting for rural loading

The effect of increasing the cost of each HMR by 10% is shown in Table 126. The estimates of QOL, drug costs and remaining health care service costs are unchanged from the baseline scenario. Consequently, as the cost of the HMR increased the ICER for this scenario was $201723 per QALY gained, which was greater than the baseline estimate.

TABLE 126 - SCENARIO ANALYSIS - EFFECT OF INCREASING TOTAL COST OF HMR BY 10% TO ACCOUNT FOR RURAL LOADING PAYMENTS

PARAMETER	WITHOUT HMR	WITH HMR	CHANGE *	TEST RESULT†
Days of ill health	8.0	7.2	0.9	*Z*=-5.455, *P*<0.001
Disability incurred (QALY)	0.013	0.011	0.001	*Z*=-5.057, *P*<0.001
Annual drug costs ($)	3 405.52	3 379.43	26.09	*Z*=-1.814, *P*=0.070
Number of GP visits	5.9	5.4	0.5	*Z*=-6.110, *P*<0.001
Cost of GP visits ($)	171.20	155.87	15.33	*Z*=-6.235, *P*<0.001
Number of specialist visits	0.4	0.3	0.0	*Z*=-5.160, *P*<0.001
Cost of specialist visits ($)	21.34	18.97	2.37	*Z*=-5.426, *P*<0.001
Cost of investigations ($)	79.81	70.91	8.91	*Z*=-6.581, *P*<0.001
Days hospitalised	0.3	0.3	0.0	*Z*=-4.483, *P*<0.001
Cost of hospitalisation ($)	316.07	282.97	33.09	*Z*=-4.616, *P*<0.001
Cost of HMR ($)	0.00	356.18	-356.18	-
TOTAL COSTS ($)	3 993.95	4 264.33	-270.39	*Z*=6.508, *P*<0.001

* Negative numbers indicate increased cost †Wilcoxon Signed Rank tests

Resampling the data for this scenario (Figure 67 Appendix XXIII) indicated a 10.2% probability of cost-effectiveness at a threshold of $150 000 per QALY gained, with zero probability of the HMRs being highly cost-effective.

The CEAC for this scenario is shown in Figure 47.

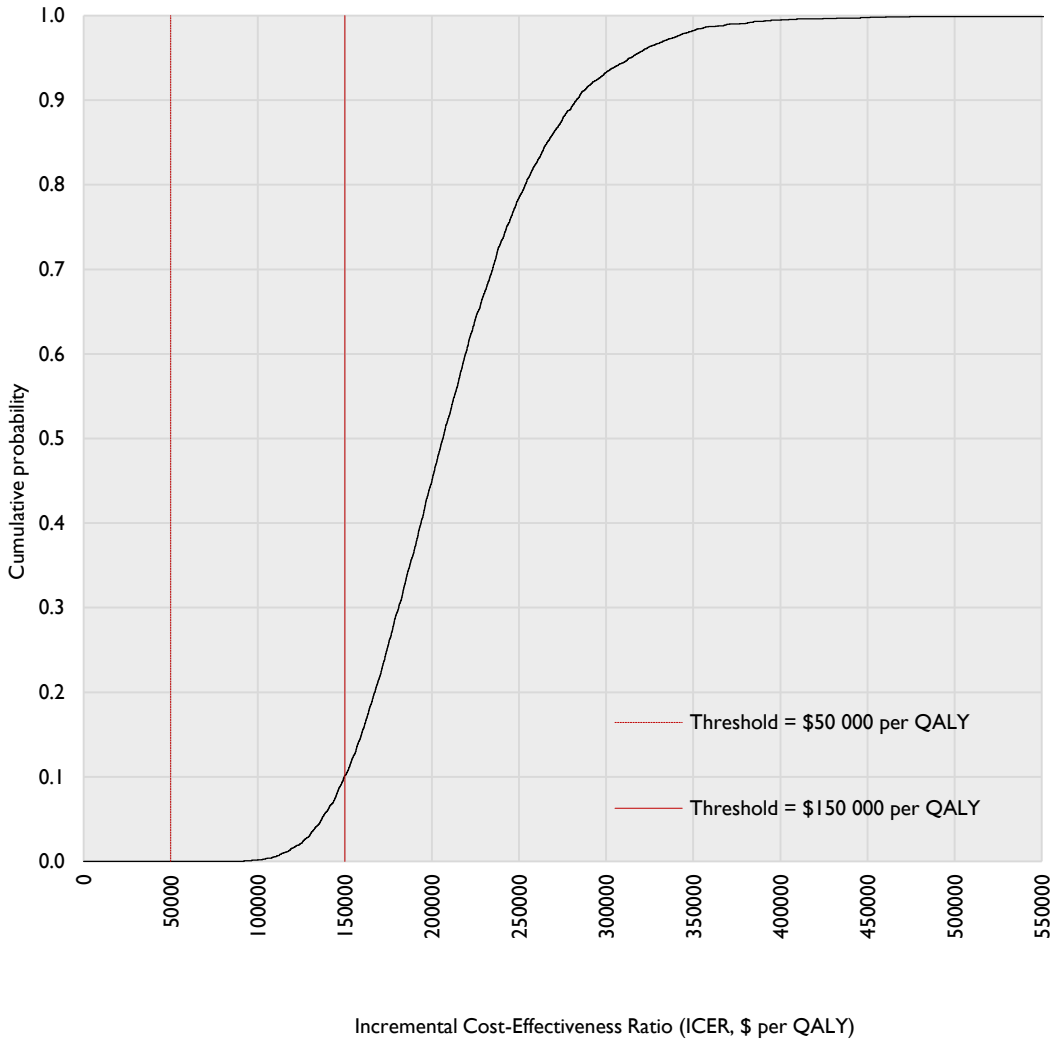

FIGURE 47 - COST-EFFECTIVENESS ACCEPTABILITY CURVE, GENERATED USING RESAMPLED DATA: HMR COST INCREASED BY 10%

6.4.3.2 Cost-effectiveness of the pharmacist component

In contrast, reducing the cost of each HMR to the amount paid to the community pharmacy resulted in an ICER of $72969 per QALY gained. As with the previous scenario, the estimates of QOL, drug costs and remaining health care service costs were unchanged from the baseline scenario, and are shown in Table 127.

TABLE 127 - SCENARIO ANALYSIS - EFFECT OF DECREASING COST OF HMR TO $183.60 (PHARMACY REIMBURSEMENT ONLY)

PARAMETER	WITHOUT HMR	WITH HMR	CHANGE *	TEST RESULT†
Days of ill health	8.0	7.2	0.9	*Z*=-5.455, *P*<0.001
Disability incurred (QALY)	0.013	0.011	0.001	*Z*=-5.057, *P*<0.001
Annual drug costs ($)	3 405.52	3 379.43	26.09	*Z*=-1.814, *P*=0.070
Number of GP visits	5.9	5.4	0.5	*Z*=-6.110, *P*<0.001
Cost of GP visits ($)	171.20	155.87	15.33	*Z*=-6.235, *P*<0.001
Number of specialist visits	0.4	0.3	0.0	*Z*=-5.160, *P*<0.001
Cost of specialist visits ($)	21.34	18.97	2.37	*Z*=-5.426, *P*<0.001
Cost of investigations ($)	79.81	70.91	8.91	*Z*=-6.581, *P*<0.001
Days hospitalised	0.3	0.3	0.0	*Z*=-4.483, *P*<0.001
Cost of hospitalisation ($)	316.07	282.97	33.09	*Z*=-4.616, *P*<0.001
Cost of HMR ($)	0.00	183.60	-183.60	-
TOTAL COSTS ($)	3 993.95	4 091.75	-97.81	*Z*=4.365, *P*<0.001

* Negative numbers indicate increased cost †Wilcoxon Signed Rank tests

The results of resampling the data in this scenario are shown in Figure 68 (Appendix XXIII). The CEAC indicated a probability of cost-effectiveness of 98.8% at a threshold of $150 000 per QALY gained, with 9.3% probability of the HMRs being highly cost-effective (Figure 48).

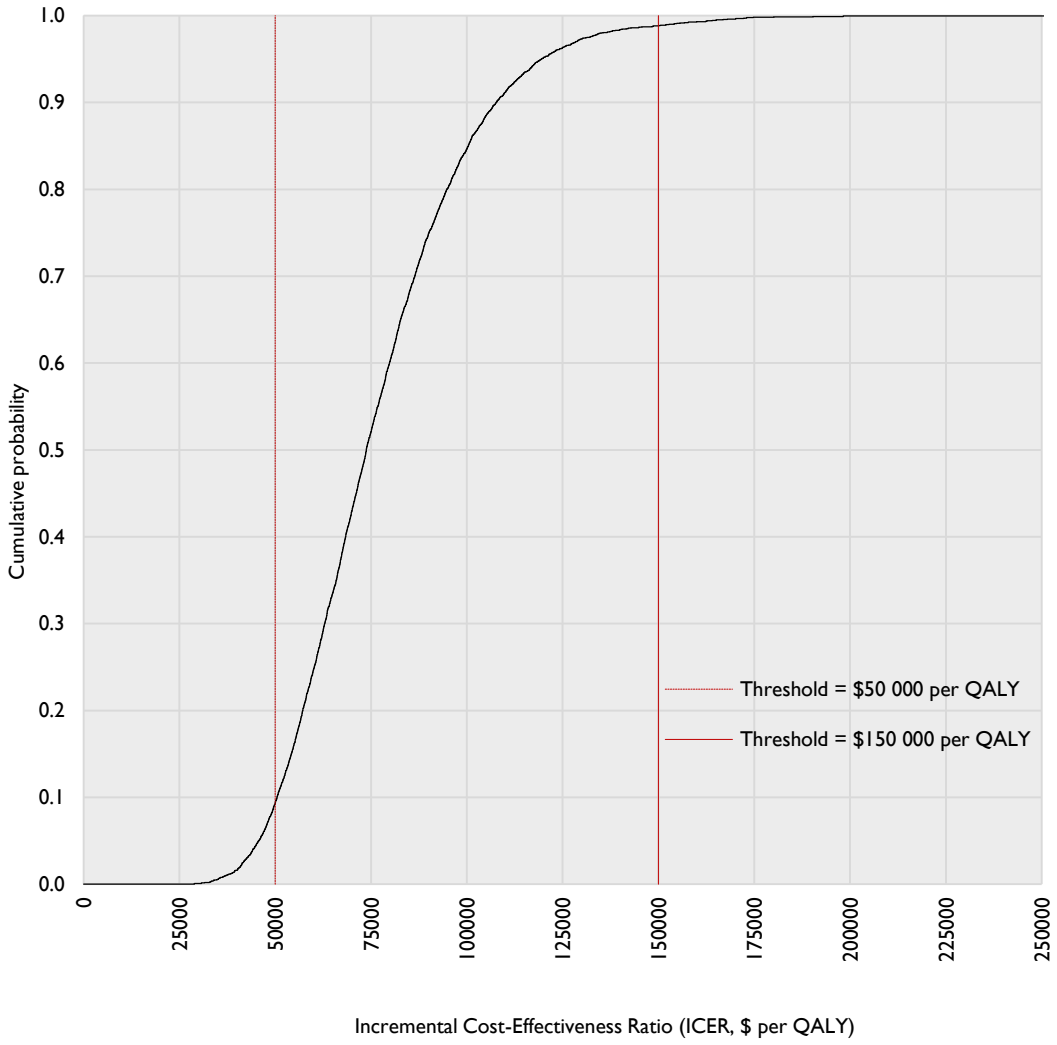

FIGURE 48 - COST-EFFECTIVENESS ACCEPTABILITY CURVE, GENERATED USING RESAMPLED DATA: PHARMACY PAYMENT ONLY

6.4.4 Attribution to the pharmacist

Predictably, removal of the *Attribution* component of the model resulted in a lower ICER compared to the baseline scenario. Table 128 shows the estimated costs and QOL effects resulting from the HMRs in this scenario, and the ICER was $62097 per QALY gained. However, as discussed by Tenni,[204] the inclusion of attribution in models that use expert opinion to value pharmacists' interventions is necessary, otherwise an overestimate of the value of the intervention is likely to be made.

TABLE 128 - SCENARIO ANALYSIS - EFFECT OF REMOVING THE *ATTRIBUTION* COMPONENT FROM THE MODEL

PARAMETER	WITHOUT HMR	WITH HMR	CHANGE *	TEST RESULT†
Days of ill health	8.8	7.2	1.7	*Z*=-5.492, *P*<0.001
Disability incurred (QALY)	0.014	0.011	0.003	*Z*=-5.168, *P*<0.001
Annual drug costs ($)	3 421.03	3 379.43	41.60	*Z*=-1.015, *P*=0.310
Number of GP visits	6.3	5.4	0.9	*Z*=-6.213, *P*<0.001
Cost of GP visits ($)	184.39	155.87	28.52	*Z*=-6.228, *P*<0.001
Number of specialist visits	0.4	0.3	0.1	*Z*=-5.322, *P*<0.001
Cost of specialist visits ($)	23.51	18.97	4.54	*Z*=-5.595, *P*<0.001
Cost of investigations ($)	87.91	70.91	17.00	*Z*=-6.603, *P*<0.001
Days hospitalised	0.4	0.3	0.1	*Z*=-4.542, *P*<0.001
Cost of hospitalisation ($)	348.09	282.97	65.12	*Z*=-4.734, *P*<0.001
Cost of HMR ($)	0.00	323.80	-323.80	-
TOTAL COSTS ($)	4 064.94	4 231.95	-167.02	*Z*=-4.167, *P*<0.001

* Negative numbers indicate increased cost †Wilcoxon Signed Rank tests

Resampling of the data (Figure 69 Appendix XXIII) indicated a 9.7% probability of cost-effectiveness at a threshold of $50 000 per QALY gained and 100% probability at $150 000 per QALY (Figure 49).

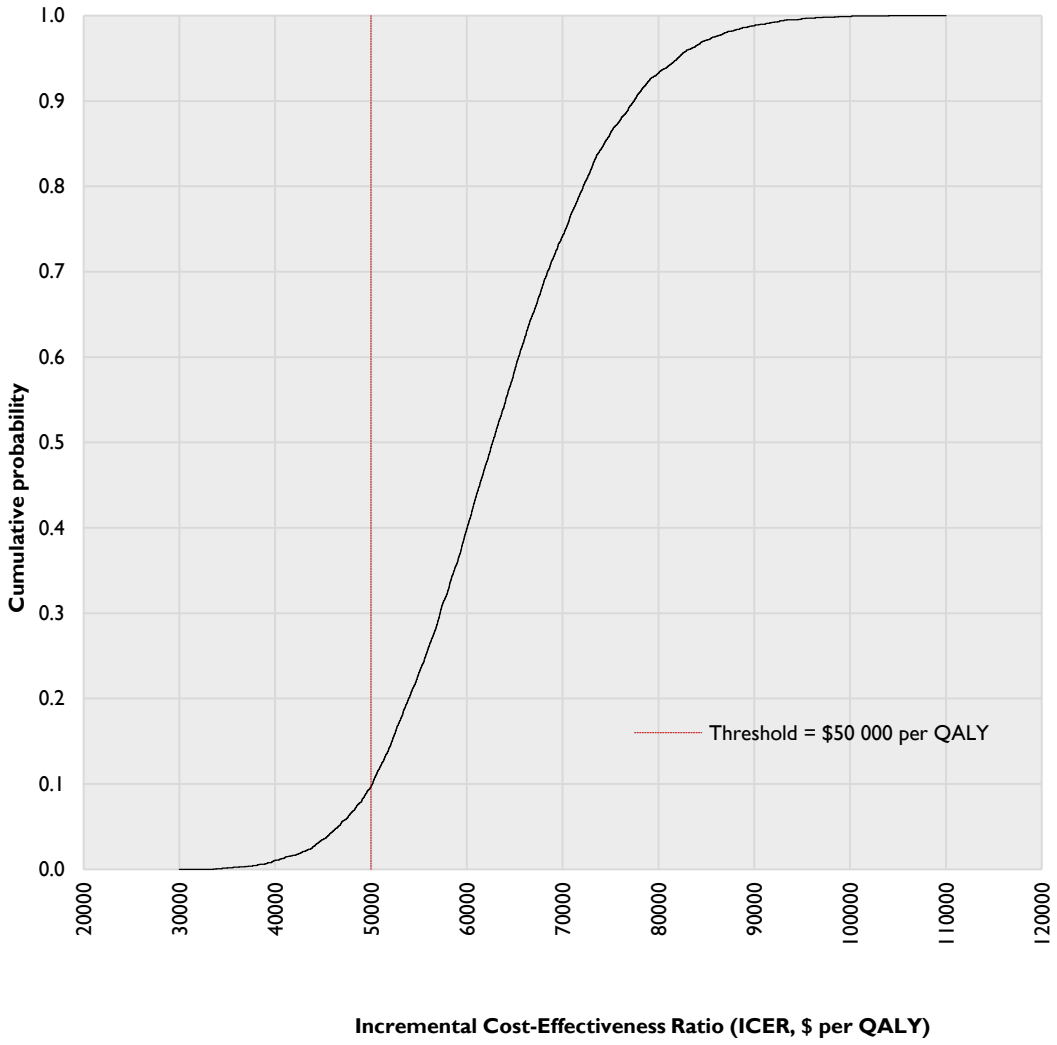

FIGURE 49 - COST-EFFECTIVENESS ACCEPTABILITY CURVE, GENERATED USING RESAMPLED DATA: *ATTRIBUTION* COMPONENT REMOVED FROM MODEL

6.4.5 Uptake of recommendations

6.4.5.1 Increased proportion of implemented recommendations

Assuming that all of the pharmacists' recommendations were enacted by the GP did not substantially affect the results of the analysis in comparison to the baseline scenario (Table 129). This potentially resulted from the relatively high proportion of recommendations that were addressed in the HMRs (in excess of 80%). Nonetheless, the expert panel's estimates indicated that, had all of the recommendations been enacted by the GP, greater savings would have been realised than in the baseline

scenario. The average saving per HMR in this scenario was $100.43, and the average gain in QOL was 0.002 QALYs per patient.

TABLE 129 - SCENARIO ANALYSIS - EFFECT OF IMPLEMENTATION OF EVERY RECOMMENDATION MADE IN THE HMR

PARAMETER	WITHOUT HMR	WITH HMR	CHANGE *	TEST RESULT†
Days of ill health	7.9	6.9	1.0	*Z*=-5.632, *P*<0.001
Disability incurred (QALY)	0.012	0.011	0.002	*Z*=-4.829, *P*<0.001
Annual drug costs ($)	3405.30	3392.08	13.22	*Z*=-3.055, *P*=0.002
Number of GP visits	5.8	5.2	0.6	*Z*=-6.434, *P*<0.001
Cost of GP visits ($)	167.91	148.69	19.22	*Z*=-6.302, *P*<0.001
Number of specialist visits	0.3	0.3	0.0	*Z*=-5.345, *P*<0.001
Cost of specialist visits ($)	20.84	17.84	3.00	*Z*=-5.580, *P*<0.001
Cost of investigations ($)	77.87	66.61	11.25	*Z*=-6.515, *P*<0.001
Days hospitalised	0.3	0.3	0.04	*Z*=-4.527, *P*<0.001
Cost of hospitalisation ($)	309.64	268.67	40.97	*Z*=-4.557, *P*<0.001
Cost of HMR ($)	0.00	323.80	-323.80	-
TOTAL COSTS ($)	3 981.78	4 205.05	-223.27	*Z*=-6.618, *P*<0.001

* Negative numbers indicate increased cost †Wilcoxon Signed Rank tests

The ICER for this scenario was $143 574 per QALY gained. Resampling the data (Figure 70 Appendix XXIII) indicated a 0% probability of cost-effectiveness at $50 000 per QALY gained. The probability of cost-effectiveness was 54.8% at a threshold of $150 000 per QALY gained (Figure 50).

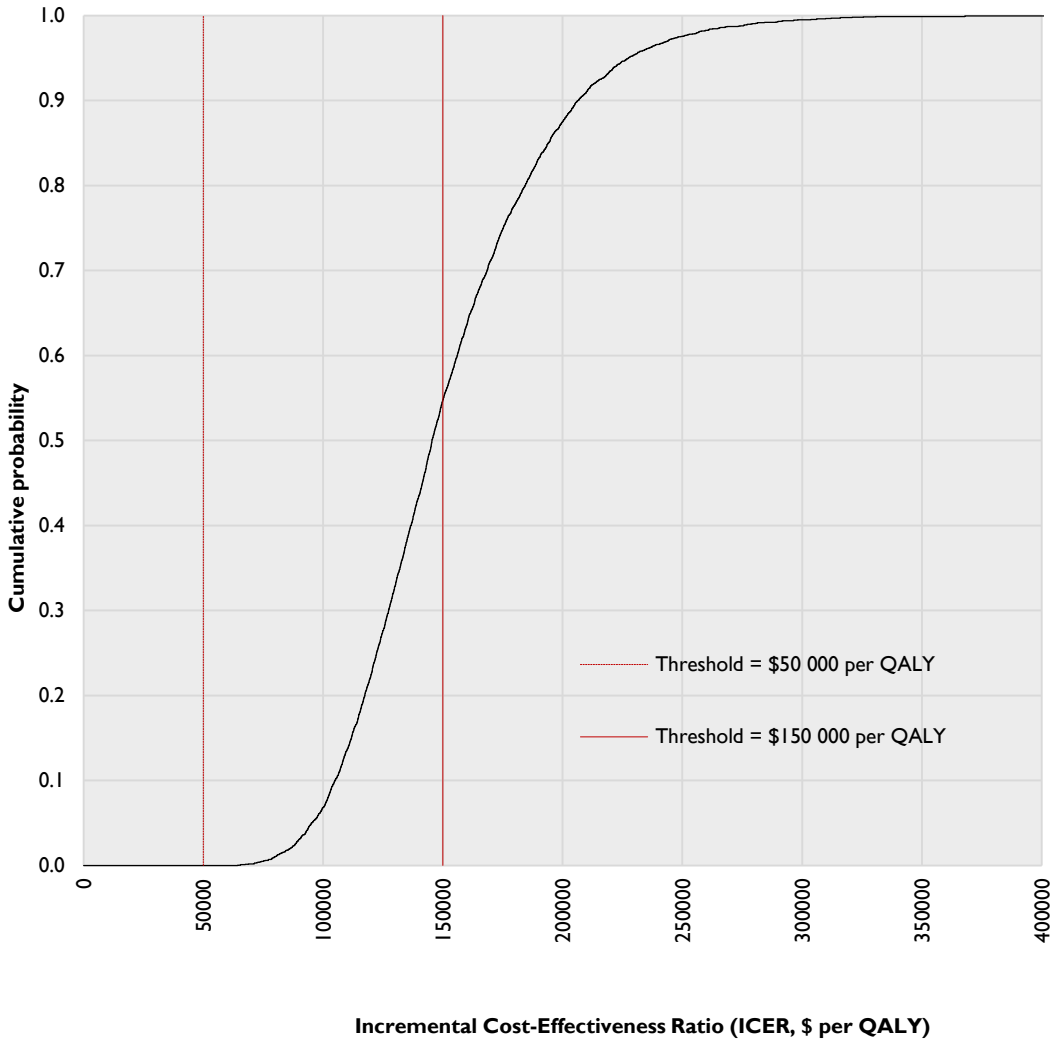

FIGURE 50 - COST-EFFECTIVENESS ACCEPTABILITY CURVE, GENERATED USING RESAMPLED DATA: ASSUMES EVERY RECOMMENDATION MADE BY PHARMACISTS WAS ENACTED BY GPS.

6.4.5.2 Decreased proportion of implemented recommendations

The study that reported the lowest proportion of the pharmacists' recommendations that were implemented was QUMCIT,[86] where 42% were implemented. The effect of reducing the proportion of recommendations with unknown outcomes to the VALMER study dataset is shown in Table 130. The average saving per HMR in this scenario was $80.34, and the average gain in QOL was 0.001 QALYs per patient. The ICER for this scenario was $195 229 per QALY gained.

TABLE 130 - SCENARIO ANALYSIS - EFFECT OF REDUCING THE PROPORTION OF IMPLEMENTED RECOMMENDATIONS WITH UNKNOWN OUTCOMES

PARAMETER	WITHOUT HMR	WITH HMR	CHANGE *	TEST RESULT†
Days of ill health	8.1	7.3	0.8	*Z*=-5.3, *P*<0.001
Disability incurred (QALY)	0.013	0.011	0.001	*Z*=-5.013, *P*<0.001
Annual drug costs ($)	3 405.52	3 379.43	26.09	*Z*=-1.814, *P*=0.070
Number of GP visits	5.9	5.5	0.5	*Z*=-6.095, *P*<0.001
Cost of GP visits ($)	171.89	157.53	14.36	*Z*=-6.272, *P*<0.001
Number of specialist visits	0.4	0.3	0.0	*Z*=-5.138, *P*<0.001
Cost of specialist visits ($)	21.45	19.25	2.20	*Z*=-5.359, *P*<0.001
Cost of investigations ($)	80.55	72.56	7.99	*Z*=-6.522, *P*<0.001
Days hospitalised	0.3	0.3	0.0	*Z*=-4.314, *P*<0.001
Cost of hospitalisation ($)	318.95	289.25	29.69	*Z*=-4.476, *P*<0.001
Cost of HMR ($)	0.00	323.80	-323.80	-
TOTAL COSTS ($)	3 998.37	4 241.83	243.46	*Z*=-5.919, *P*<0.001

* Negative numbers indicate increased cost †Wilcoxon Signed Rank tests

Resampling of the data (Figure 71 Appendix XXIII) indicated a 0% probability of cost-effectiveness at $50 000 per QALY gained. The CEAC for this scenario is shown in Figure 51.

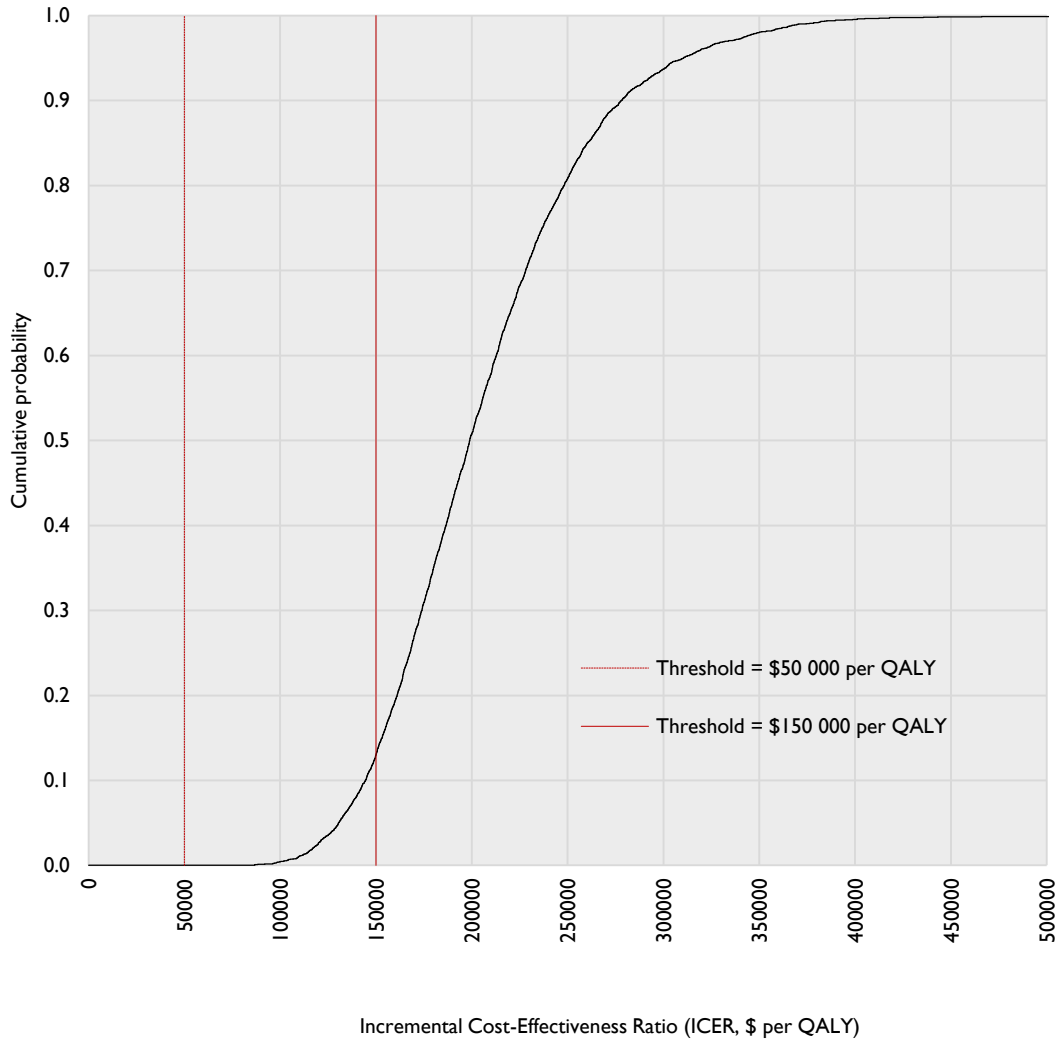

FIGURE 51 - COST-EFFECTIVENESS ACCEPTABILITY CURVE, GENERATED USING RESAMPLED DATA: ASSUMES 42% PROBABILITY THAT RECOMMENDATIONS MADE BY PHARMACISTS WITH UNKNOWN OUTCOMES WERE ENACTED BY GPS.

6.4.6 Best case - inclusion of DRPs not assessed by experts

In the baseline scenario, only the first three DRPs identified in the HMR reports were assessed by the experts. However, the mean number of DRPs documented in the HMR reports was 3.5 (SD ±1.8, range 0-13); hence, a substantial number of the DRPs in the baseline scenario were valued at zero. To generate the "best case" scenario, the DRPs not included in the expert assessment were valued at the average value of the DRPs assessed by the experts in the baseline scenario. To account for the possibility that these DRPs may have been of lower clinical significance (and therefore less valuable)

than the first three DRPs addressed in the HMRs, the average DRP value was discounted by 25%, 50% and 75%, respectively.

The results for these scenarios are shown in Table 131. The ICER for each scenario was below $150 000, although none approached $50 000.

TABLE 131 - SCENARIO ANALYSIS- INCLUSION OF DRPS NOT VALUED IN BASELINE SCENARIO

PARAMETER	VALUE OF ADDITIONAL DRPS											
	100% OF AVERAGE DRP VALUE			75% OF AVERAGE DRP VALUE			50% OF AVERAGE DRP VALUE			25% OF AVERAGE DRP VALUE		
	WITHOUT HMR	WITH HMR	TEST RESULT†	WITHOUT HMR	WITH HMR	TEST RESULT†	WITHOUT HMR	WITH HMR	TEST RESULT†	WITHOUT HMR	WITH HMR	TEST RESULT†
Days of ill health	13.3	11.9	*Z*=-6.493, *P*<0.001	12.0	10.7	*Z*=-6.538, *P*<0.001	10.7	9.5	*Z*=-6.250, *P*<0.001	9.3	8.3	*Z*=-6.103, *P*<0.001
Disability incurred (QALY)	0.021	0.019	*Z*=-6.213, *P*<0.001	0.019	0.017	*Z*=-6.236, *P*<0.001	0.017	0.015	*Z*=-5.845, *P*<0.001	0.015	0.013	*Z*=-5.725, *P*<0.001
Annual drug costs ($)	3 397.59	3 371.50	*Z*=-1.814, *P*=0.070	3 399.57	3 373.48	*Z*=-2.054, *P*=0.040	3 401.56	3 375.47	*Z*=-1.814, *P*=0.070	3 403.54	3 377.45	*Z*=-2.054, *P*=0.040
Number of GP visits	9.8	9.0	*Z*=-6.662, *P*<0.001	8.8	8.1	*Z*=-6.741, *P*<0.001	7.9	7.2	*Z*=-6.611, *P*<0.001	6.9	6.3	*Z*=-6.601, *P*<0.001
Cost of GP visits ($)	284.30	258.84	*Z*=-6.596, *P*<0.001	256.02	233.10	*Z*=-6.685, *P*<0.001	227.75	207.36	*Z*=-6.530, *P*<0.001	199.47	181.61	*Z*=-6.559, *P*<0.001
Number of specialist visits	0.59	0.52	*Z*=-6.397, *P*<0.001	0.53	0.47	*Z*=-6.419, *P*<0.001	0.47	0.42	*Z*=-6.198, *P*<0.001	0.41	0.37	*Z*=-5.977, *P*<0.001
Cost of specialist visits ($)	35.4	31.5	*Z*=-6.449, *P*<0.001	31.9	28.4	*Z*=-6.489, *P*<0.001	28.4	25.2	*Z*=-6.228, *P*<0.001	24.9	22.1	*Z*=-6.117, *P*<0.001
Cost of investigations ($)	132.54	117.75	*Z*=-6.729, *P*<0.001	119.36	106.04	*Z*=-6.839, *P*<0.001	106.18	94.33	*Z*=-6.729, *P*<0.001	93.00	82.62	*Z*=-6.839, *P*<0.001
Days hospitalised	0.5	0.5	*Z*=-5.941, *P*<0.001	0.5	0.4	*Z*=-5.956, *P*<0.001	0.4	0.4	*Z*=-5.595, *P*<0.001	0.4	0.3	*Z*=-5.437, *P*<0.001
Cost of hospitalisation ($)	524.86	469.91	*Z*=-6.088, *P*<0.001	472.67	423.18	*Z*=-6.047, *P*<0.001	420.47	376.44	*Z*=-5.668, *P*<0.001	368.27	329.71	*Z*=-5.486, *P*<0.001
Cost of HMR ($)	-	323.80	-	-	323.80		-	323.80	-	-	323.80	-
TOTAL COSTS ($)	4 374.74	4 573.31	*Z*=-5.816, *P*<0.001	4 279.54	4 487.97	*Z*=-5.985, *P*<0.001	4 184.34	4 402.63	*Z*=-6.147, *P*<0.001	4 089.14	4 317.29	*Z*=-6.287, *P*<0.001
ICER ($ per QALY)		89 210			103 980			122 419			146 084	

* Negative numbers indicate increased cost †Wilcoxon Signed Rank tests

The resampled ICER data are shown in Figure 72 to Figure 75 (Appendix XXIII), and the CEACs are shown in Figure 52.

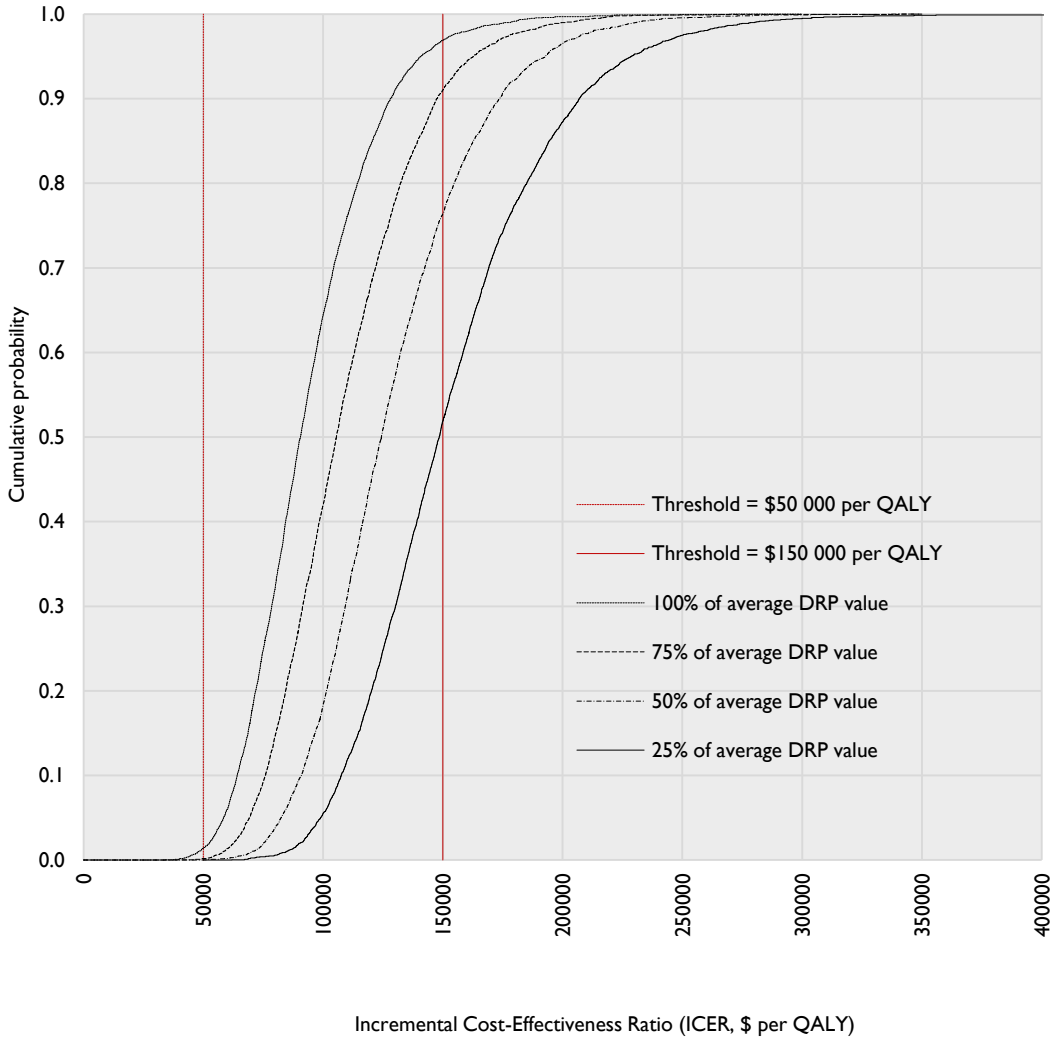

FIGURE 52 - COST-EFFECTIVENESS ACCEPTABILITY CURVE, GENERATED USING RESAMPLED DATA: INCLUSION OF DRPS NOT VALUED BY EXPERTS

For these scenarios, a summary of the probabilities of cost-effectiveness at thresholds of $50 000 and $150 000 per QALY gained is shown in Table 132.

TABLE 132 - PROBABILITIES OF COST-EFFECTIVENESS WHEN DRPS NOT VALUED BY EXPERTS INCLUDED IN MODEL

VALUE OF ADDITIONAL DRPS (% OF AVERAGE DRP VALUE)	ICER ($ PER QALY GAINED)	PROBABILITY OF COST-EFFECTIVENESS AT THRESHOLD	
		$50 000 PER QALY GAINED	$150 000 PER QALY GAINED
100%	89 210	13.8	96.9
75%	103 980	1.8	91.0
50%	122 419	0.0	76.4
25%	146 084	0.0	51.9

6.4.7 Worst case

For the worst case scenario, the baseline cost was increased by 10% to account for rural loading, and the probability of recommendations with unknown implementation used was the lowest reported in the HMR literature (42%). The average saving per HMR in this scenario was $79.52, and the average gain in QOL was 0.001 QALYs per patient (Table 133). The ICER for this scenario was $225 462 per QALY gained.

TABLE 133 - SCENARIO ANALYSIS- WORST CASE SCENARIO

PARAMETER	WITHOUT HMR	WITH HMR	CHANGE *	TEST RESULT†
Days of ill health	8.1	7.3	0.8	*Z*=-5.3, *P*<0.001
Disability incurred (QALY)	0.013	0.011	0.001	*Z*=-5.013, *P*<0.001
Annual drug costs ($)	3 405.52	3 379.43	26.09	*Z*=-1.814, *P*=0.070
Number of GP visits	5.9	5.5	0.5	*Z*=-6.095, *P*<0.001
Cost of GP visits ($)	172.01	157.78	14.23	*Z*=-6.272, *P*<0.001
Number of specialist visits	0.4	0.3	0.0	*Z*=-5.138, *P*<0.001
Cost of specialist visits ($)	21.50	19.35	2.15	*Z*=-5.359, *P*<0.001
Cost of investigations ($)	80.77	72.98	7.79	*Z*=-6.522, *P*<0.001
Days hospitalised	0.3	0.3	0.0	*Z*=-4.314, *P*<0.001
Cost of hospitalisation ($)	319.35	290.08	29.27	*Z*=-4.476, *P*<0.001
Cost of HMR ($)	0.00	356.18	-356.18	-
TOTAL COSTS ($)	3 999.14	4 275.79	276.66	*Z*=-5.919, *P*<0.001

* Negative numbers indicate increased cost †Wilcoxon Signed Rank tests

The resampled data is shown in Figure 76 (Appendix XXIII). For this scenario, the probability of cost-effectiveness at $150 000 per QALY gained was 5% (Figure 53).

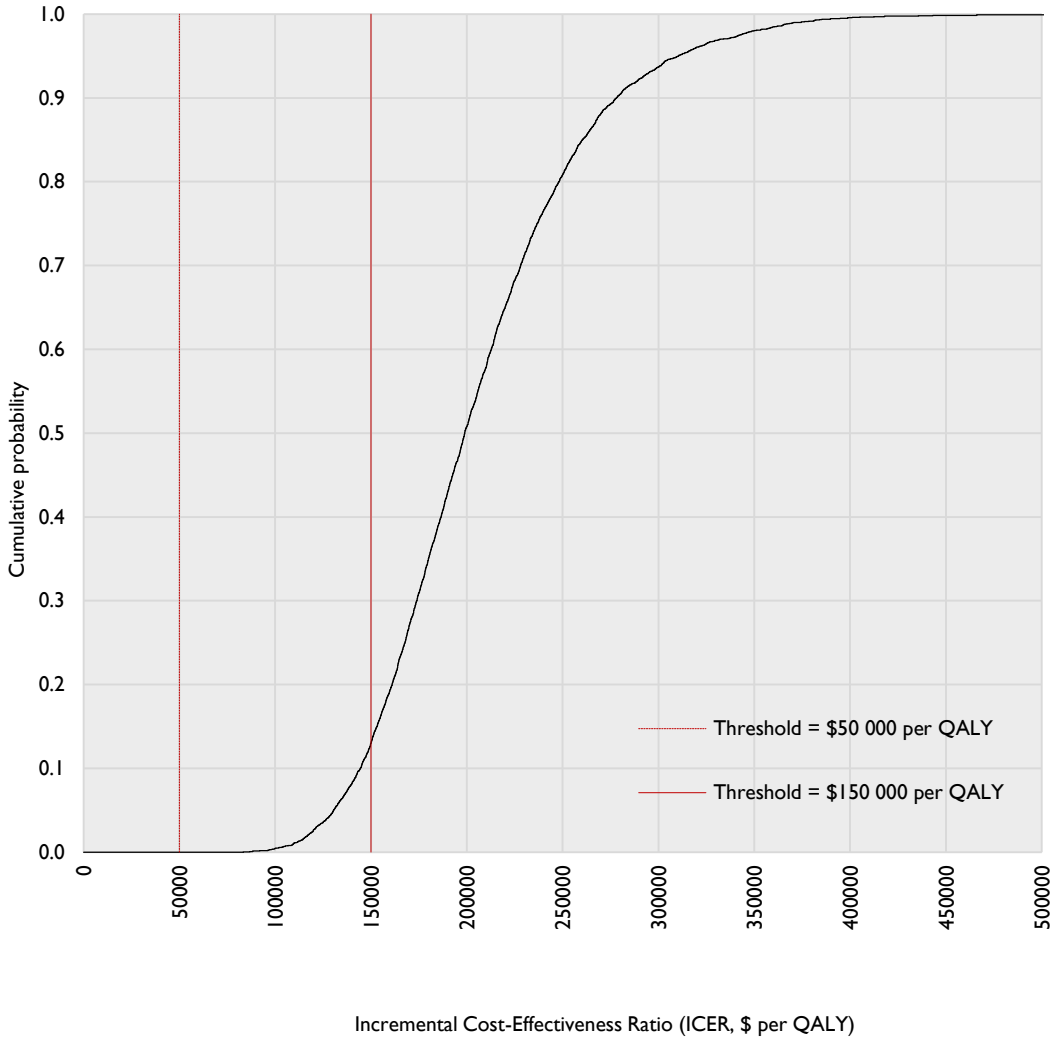

FIGURE 53 - COST-EFFECTIVENESS ACCEPTABILITY CURVE, GENERATED USING RESAMPLED DATA: WORST CASE

6.5 Summary of results

In summary, the economic analysis identified the following:

- Compared to usual care, the HMRs did not result in significantly reduced drug costs. The average annual drug cost saving was $1.25 per patient.
- Had all of the pharmacists' recommendations been implemented, the HMRs were estimated to have resulted in a non-significant increase of $2.24 per patient in annual drug costs compared to usual care.
- There were differences between drug classes in terms of the increased costs and savings resulting from the HMRs. The drug classes associated with the greatest savings were drugs that treat disorders of the *Alimentary tract and metabolism* and *Musculoskeletal system*. Drugs that treat disorders of the *Respiratory system* were responsible for the greatest net increase in drug costs.
- The clinical outcomes most frequently affected by the HMRs were *Pain*, *Confusion*, *Renal dysfunction*, *Myocardial ischaemia* and *Gastrointestinal bleeding*. The HMRs were estimated to result in significantly reduced likelihoods of *Arrhythmias*, *Confusion* and *Myopathy* all severity levels ($P<0.05$), *Allergic reaction*, *Asthma* and *Renal dysfunction* at *Severe* levels, and the *Mild* and *Moderate* levels of *Osteoporosis*. However, the magnitude of the potential improvements in the clinical outcomes was small.
- It was estimated that the HMRs would not significantly increase the risk of any consequence occurring at any level of severity.
- The HMRs were estimated to result in significant savings to the healthcare system from reduced GP and specialist visits, laboratory/ pathology investigations and hospitalisations.
- The estimates of the savings generated by the HMRs were insufficient to offset the additional cost incurred by providing the HMRs in the 12 months following the HMR. Sensitivity analysis indicated that the average net cost of a HMR ranged between $198.57 and $276.65.
- The majority of the estimated savings occurred in a small number of HMRs, with 6.7% of the HMRs offsetting costs in the baseline scenario.
- The HMRs were also estimated to result in a small but significant improvement in QOL compared to usual care (average 0.001 QALY per patient at the baseline scenario). There was no relationship between HMRs in which QOL was substantially improved and those resulting in the greatest savings.

- The DRP type with the greatest estimated benefit on QOL involved *Untreated indications*. The resolution of *Toxicity* DRPs was potentially detrimental to QOL. Differences between DRP types and potential savings were not identified.
- At the conservative baseline scenario, the cost-utility analysis found a probability of cost-effectiveness compared to usual care of 22.2% at a threshold of $150000 per QALY gained.
- Sensitivity analysis indicated that the probability of cost-effectiveness of HMRs ranged from 5% to 97% at a threshold of $150000 per QALY gained.
- Based on the results of the cost-utility analysis, the total cost of a HMR would have to be reduced substantially for HMRs to be considered cost-effective or highly cost-effective according to WHO thresholds. At the baseline scenario, HMRs would need to cost a maximum of $286.85 to be cost-effective, or $152.81 to be highly cost-effective. At the least conservative best case scenario, the total cost would need to be reduced to $212.51 for HMRs to be highly cost-effective (the ICER was below $150 000 per QALY gained in this scenario).

Chapter 7 - Discussion and conclusions of the VALMER study

The VALMER study provided some important insight into the nature of the interventions made in HMRs, the potential clinical outcomes of these interventions and their cost-effectiveness. Whilst the findings regarding the cost-effectiveness of HMRs raised questions as to whether the HMR program is an appropriate use of funding as it is currently implemented, the study identified that some individual HMRs are likely to be highly cost-effective, and may significantly reduce the risk of a number of important clinical consequences.

In interpreting the findings of the study in the context of the existing literature involving MMRs, consideration must be given to the similarities and differences between studies in the MMR model, the DRPs identified, and the methodologies employed to measure outcomes.

7.1 Drug-related problems

Based on the findings of existing literature, the general characteristics of the patients who received HMRs in the VALMER study indicated that the majority of them were considered to be at high risk of ADEs. Risk factors for ADEs commonly identified in previous research include increasing age, multiple chronic medical problems, taking multiple medications, and taking "high-risk" medications.[8] In Australia, Burgess *et al*. found that the rate of ADR-related hospitalisations increased substantially with age- from 7.7 per 1000 person-years for patients aged between 60 and 69 years, to 34.3 per 1000 person-years at ages 80 years and over.[11] More recently, Budnitz *et al*. reported that 48.1% of emergency hospitalisations in adults aged 65 years or older in the USA occurred in patients aged 80 years or more, despite this demographic accounting for less than 20% of the population.[257] An international systematic review of the prevalence of ADEs in patients of all ages in ambulatory care found a median preventable ADE rate of 3.45%, with the rate being 16.1% in elderly patients.[258] The median age of the patients in the VALMER study was 78 years, which would seem to stratify them into a high-risk age category based on these studies.

In addition to their advanced age, the VALMER study patients were diagnosed with multiple chronic conditions and consequently they were taking numerous medications. Several previous studies have associated a greater number of medications with an increased likelihood of DRPs, including ADEs. [118, 119, 259, 260] More importantly, a substantial number of the patients in the study were taking medications that have been identified as resulting in a high risk of ADEs. These high-risk medications include drugs affecting the cardiovascular system (such as diuretics, ACE-inhibitors and digoxin), antithrombotic agents (such as warfarin), musculoskeletal drugs (commonly non-steroidal anti-inflammatory drugs), oral hypoglycaemic agents, and psychotropic medications such as anti-cholinergics, benzodiazepines, antipsychotics, sedatives and hypnotics.[8, 257] Therefore, on face value, it may be concluded that the patients who received HMRs appeared to be those individuals whom guidelines indicate would benefit the most from the service. As a consequence, the pharmacists identified a substantial number of DRPs in the HMRs.

The mean number of DRPs documented per HMR was 3.5, which was consistent with the findings of several past Australian and international studies of MMRs which ranged from 1.3[60] to 8.2[27] DRPs per review. The relative frequencies of the types of DRPs identified in the VALMER study were also consistent with the findings of previous literature. Nearly half of the patients (45%) were documented with at least one DRP relating to compliance or concordance, and almost as many (39%) were identified as experiencing a suspected or actual ADE. These two DRP types each accounted for 14% of all DRPs documented. Of even greater prevalence were patients with conditions treated either inadequately or not at all, which was documented in 76% of patients (27.5% of DRPs).

These frequencies are generally consistent with those reported in previous studies of HMRs. In consideration of the Australian QUM Evaluation Program Projects discussed in Section 1.3.1, the proportions of DRP types were most consistent with those reported in the QUMCIT.[86] In that study, compliance issues were the most common DRP type (approximately 33% of DRPs identified), followed by the need for additional therapy (24.9% of DRPs, 50% of patients). In contrast, the proportion of DRPs resulting from untreated indications in the other studies ranged from 1.5% to 6.3%.[66, 140] Despite these differences, the proportion of ADE DRPs in the VALMER study was comparable to the results reported in the QUM Evaluation Program Projects, which

ranged from 10.4% to 16.9% of DRPs.[86, 140] More recent retrospective studies of HMRs reported that between 9.5% and 19% of the DRPs identified in the HMRs were ADEs.[55, 68] In consideration of these results, it is apparent that the frequencies of DRP types identified in HMRs have not changed substantially since the program's implementation. Consequently, it seems reasonable to have anticipated that the outcomes of the HMRs in the VALMER study would be similar to those reported previously.

Further evidence of this is that several of the drug groups frequently associated with the DRPs were amongst those considered to be "high-risk". Approximately half of the patients taking warfarin, digoxin or non-steroidal anti-inflammatory drugs were documented with a DRP related to those drugs (43.6%, 51.8% and 60.0% respectively). Similarly, DRPs relating to ACE inhibitor/ angiotensin II receptor antagonists or diuretics were identified in approximately one third of patients taking these drugs (38.9% and 36.4%, respectively). Budnitz *et al*. reported that warfarin was implicated in 33% of ADE-related hospital admissions in the USA between 2007 and 2009, digoxin in 3.5% of admissions, and ACE inhibitor/ angiotensin II receptor antagonists in 3%.[257] Onder *et al*. found that diuretics was the drug class most frequently implicated in ADE-related hospitalisations in older Italian patients, responsible for 17.3% of these hospitalisations.[261] In Australia, NSAIDs have been associated with a significantly increased risk of hospitalisation in patients taking these drugs (incidence rate ratio 1.5, 95% CI 1.3 to 1.6).[262] These four drug classes were also identified as the most common causes of ADE-related hospitalisations in the UK.[263]

The frequencies of the types of recommendations made by the pharmacists to resolve the DRPs in the VALMER study were also reasonably consistent with the results of previous research. The most common recommendation was for additional laboratory monitoring, which accounted for 18% of all recommendations made by the pharmacists. In previous studies of HMRs, the frequency of recommendations for increased monitoring ranged between 14% and 22%.[27, 55] The higher frequency of recommendations to intensify therapy compared to recommendations to reduce treatment (26% versus 19%) was also consistent with the results of some previous studies. For example, 23% of the recommendations made in a study by Castelino *et al*. were for increased doses or to commence new drugs, compared to 16% of recommendations to reduce doses or cease drugs.[55] In contrast, however, the

Sutherland project reported that recommendations to intensify therapy accounted for less than 3% of the total number of recommendations.[139]

In consideration of the similarities between the findings regarding the DRPs addressed in the VALMER study and those of previous research, it is understandable that the proportion of recommendations implemented following the HMR was also consistent with prior studies. In the VALMER study, approximately 50% of all of the pharmacists' recommendations were implemented verbatim by the GPs, and a further 8% were partially implemented. When combined with the DRPs that did not need the GPs' involvement to resolve, 82% of the DRPs were addressed in some way as a result of the HMR. This finding was aligned with the proportions of enacted recommendations reported in previous HMR studies, that ranged from 42%[126] to 90%.[27] Importantly, the study identified that high proportions of potentially resolved DRPs were also observed in DRPs involving several high-risk drugs. However, the comparatively low proportion of resolved DRPs involving anti-platelet drugs is somewhat concerning and may be a target for further research, given that a recent study associated these drugs with 13% of emergency ADE-related hospitalisations in older patient in the US.[257]

Based on the DRPs identified and the frequency with which the DRPs were resolved, it may be concluded from the results of the VALMER study that the HMRs addressed the program's objectives of achieving "*safe, effective, and appropriate use of medications by detecting and addressing DRPs that interfere with desired patient outcomes*".[19] What is concerning is that, despite the plethora of literature regarding these issues and the availability of interventions to address them (such as HMRs), the prevalence of DRPs involving these drugs does not appear to have changed appreciably in the past ten years. Although it was not an aim of the trial, the results of the VALMER study reiterate the need for programs that target DRPs in high risk populations. However, the economic analysis predicted that the current HMR program with its present funding structure may not be a cost-effective way to resolve DRPs, as discussed below.

7.2 Clinical and economic outcomes

7.2.1 Clinical outcomes

The experts estimated that, overall, the HMRs were likely to reduce the probability of a number of detrimental consequences occurring without significantly increasing the risk of any consequence. Significant reductions in the likelihood of *Arrhythmias*, *Confusion* and *Myopathy* were observed at all severity levels, whilst the mild and moderate levels of *Osteoporosis*, mild *Chronic airways disease* and severe health states of *Allergic reaction*, *Asthma* and *Renal dysfunction* were also estimated to be significantly lower as a result of the HMRs.

The reduced risk of *Confusion* was understandable, given that one of the beneficial outcomes of MMRs consistently reported in the literature has been improved patient knowledge and understanding of their medications (that is, reduced confusion).[15, 30, 100, 139] However, the reductions in the risk of *Arrhythmias* and *Myopathy* were not anticipated, as there is no evidence in the literature that MMRs may be beneficial in preventing these consequences. Analysis of the DRPs identified in the study provides some insight into the reasons for these findings. With regards to *Myopathy*, a drug class commonly implicated in causing this consequence is HMG-CoA reductase inhibitors.[264] Approximately 60% of patients in the VALMER study were taking a drug of this class, and one in four of these patients were documented as having a DRP involving it. The most frequently identified DRPs involving these drugs related to safety concerns, with *Drug interactions*, *Toxicity evident* and *Laboratory monitoring* accounting for over half of the DRPs involving these drugs. Hence, it is plausible that the pharmacists' recommendations to resolve these DRPs would account for the significant reduction in the likelihood of *Myopathy*. Interestingly, this drug class would have accounted for the greatest increase in drug costs had all of the pharmacists' recommendations been accepted, which implies that many recommendations to commence or increase doses of these drugs were also made. However, it was apparent that few of these recommendations were implemented, as the class was not responsible for substantially increased drug costs.

An explanation for the reduction in risk of *Arrhythmia* is less apparent as there is no single drug or drug class with pro-arrhythmic potential that was frequently involved

in the DRPs. Neither was the prevalence of arrhythmias in the patient population so great as to suggest that improved management would account for the benefits. To illustrate, whilst 18% of the patients were diagnosed with atrial fibrillation (generally acknowledged as the most common arrhythmia in elderly patients)[265], only 15 DRPs involving this condition were documented in total. Consequently, it is most likely that DRPs involving various drugs and diseases were responsible for the benefits. It is possible that resolution of the DRPs involving digoxin, a drug which can cause arrhythmias in overdose,[266] was responsible for some of the *Arrhythmia* benefits; DRPs involving digoxin were predominantly related to safety concerns (such as inadequate *Monitoring* and *Drug interactions*) and were frequently resolved. Further evidence of this is provided by a literature review of hospitalisations attributed to drug-drug interactions, which reported that the reason for admission for 18% of these hospitalisations was some form of cardiac rhythm disturbance.[267]

There is some evidence in the literature that pharmacist involvement may improve the management of the remaining consequences for which a reduced probability was found in the VALMER study (*Osteoporosis*, *Asthma*, *Chronic airways disease*, *Allergic reaction* and *Renal dysfunction*). It is likely that the reduction in risk of *Allergic reaction* and *Renal dysfunction* resulted from the pharmacists addressing potential and actual ADEs resulting from *Toxicity* (actual ADEs) and *Drug selection* (potential ADEs) DRPs. However, none of the consequences relating to chronic diseases were specifically targeted in studies of MMRs, nor were there reported benefits in these consequences in the general MMR literature. A recent systematic review of pharmacist interventions in osteoporosis management found that there was some evidence of benefit in terms of identification of high-risk patients and improved calcium intake.[268] A 2009 review of studies that investigated pharmacist involvement in asthma management concluded that there was no consistent benefit in clinical outcomes, however, there was some evidence that the frequency of symptoms or severity of asthma was reduced.[269]

The reduced estimated risk of severe chronic airways disease observed in the VALMER study is of particular importance for further research, as there has been some interest in expanding the role of pharmacists in managing chronic airways disease in recent years.[270] Furthermore, a recent RCT of pharmaceutical care in managing this condition found a significantly reduced chronic airways disease-related

hospital admission rate in patients who received pharmaceutical care compared to controls.[271] Based on these results, there may be an argument for an investigation of the effect of HMRs in patients with chronic airways disease. Should such a study be undertaken, it must be acknowledged that the results of the VALMER study indicate that an increase in respiratory drug costs is likely to occur.

7.2.2 Economic analysis

7.2.2.1 Comparison to previous studies

Based on these probable clinical outcomes, the VALMER study estimated that HMRs would result in $85.79 of reduced health resource utilisation in the 12 months following the review, the majority of which resulted from reduced hospitalisation costs (39%). Though there are no previous studies that have been conducted using the methodology employed in the VALMER study, general comparisons between these findings and previous research can be made. Given the diversity of the international studies that have investigated the cost-effectiveness of MMRs discussed in Chapter One of this thesis, it is perhaps most appropriate to interpret the findings of the VALMER study in the context of the Australian QUM Evaluation Program Projects. The average economic benefit found in the VALMER study is relatively small compared to these previous studies, which identified average savings ranging between approximately $130 and $400 per HMR.[66, 86, 139, 142] There are several potential reasons for these differences, including differences in drug costs, methodologies employed and the type of experts who estimated the outcomes of the HMRs.

7.2.2.1.1 Drug costs

As discussed in Chapter One, the perspective taken for the measurement of drug costs may influence the results of cost-effectiveness studies of HMRs. The perspective taken by the VALMER study was aligned with that of the Domiciliary Medication Review Project and QUMCIT, where only drug costs to the PBS were considered and drugs not PBS subsidised were not measured.[66, 86, 144] As with these two previous studies, the VALMER study identified that HMRs were unlikely to result in substantially reduced drug costs. In contrast, the remaining studies appeared to cost drugs from a patient perspective, and all reported significant savings resulting from HMRs.[136, 139, 142] Hence, the results of the VALMER study provide additional evidence that HMRs do not result

in significant savings to the PBS. Future research may investigate this possibility further by comparing the effects of HMRs on the cost of drugs from both government and patient perspectives.

A second reason for the differences in drug cost changes between the VALMER study and some of the previous studies involves the frequency of identification of DRPs likely to result in reduced drug costs. In the VALMER study, the proportion of DRPs involving too-low doses, untreated indications or requiring additional therapy was approximately 30%. As discussed in Chapter One of this thesis, similarly high proportions of these types of DRPs were identified in the Domiciliary Medication Review Project and QUMCIT, and neither of these studies associated HMRs with substantially reduced drug costs.[66, 86, 144] In contrast, the proportions of these types of DRPs in the Sutherland Project was only 1.5%, and a reduction in average monthly medication cost of approximately $20 per patient was identified. In consideration of the results of these studies, it may be concluded that HMRs do not result in substantial savings to the PBS in drug costs in the 12 months following the review.

At face value, this finding may be interpreted as an undesirable outcome of HMRs. However, it must be viewed in consideration that one of the objectives of HMRs is to address the issue of all DRPs, not simply those that may reduce drugs costs short-term. The VALMER study identified that many DRPs resulted from under-treatment of conditions, and resolving these DRPs will not reduce costs short-term. The health system must be willing to accept any potential burden imposed by resolving these DRPs as this may generate longer term cost benefits to the health system in total. A high proportion of the medications that were commenced as a result of the HMRs have proven cost-effectiveness, including many of the cardiovascular and diabetes treatments.[272-274] If a much longer time horizon was assumed, savings to the health system in both drug and health service costs were likely to have occurred in the patients in whom these DRPs were resolved.

7.2.2.1.2 Methodological differences between studies

A second potential source for the small estimated savings in the VALMER study compared to the estimates made in earlier research involves differences in the methodologies used to measure health resource costs. Firstly, whilst expert opinion

was used in the VALMER study, QUMCIT and the Sutherland Project, a higher proportion of medical practitioners as assessors were used in the VALMER study relative to these other studies. In QUMCIT, a majority of the HMRs were assessed by two pharmacists only. Similarly, in the Sutherland Project, medical practitioners accounted for half of the expert panel; in contrast, approximately three quarters of the experts in the VALMER study were medical practitioners. Two components of the VALMER data imply that pharmacists predict greater benefits resulting from HMRs than medical practitioners. Firstly, the attribution estimates of the pharmacists were significantly greater than those of the GPs and specialists, which may be interpreted as demonstrating that the pharmacist experts tended to value HMRs more than the medical practitioners. Secondly, in the comparison of the individual experts' raw estimates of the healthcare costs and QOL changes occurring in the 60 HMRs assessed by every expert (Table 112), the pharmacists' estimates seemed to indicate greater benefit than the majority of the medical practitioners. Conversely, the raw estimates of three of the seven specialist physicians indicated that the HMRs would increase healthcare service utilisation costs compared to usual care, and four of the physicians indicated that HMRs would worsen QOL. It is possible that if the expert panel used in the VALMER study had utilised a more comparable proportion of medical practitioners and pharmacists to previous studies, then the average economic benefit arising from HMRs may have been comparable.

Another significant difference in the methodology used in the VALMER study compared to previous studies involves the concept of attribution to the pharmacist. Tenni (as described by Stafford *et al*.[191]) asserted that this parameter must be considered when using expert panels to predict the outcomes of pharmacists' interventions, otherwise the estimated value of the intervention would be exaggerated.[204] The results of a RCT that investigated the effects of MMRs in elderly patients in the UK conducted by Krska *et al*. support this assertion.[47] In that study, 78.8% of DRPs identified in the study were resolved in the MMR group at follow-up, whilst 39.3% of the DRPs had been resolved in the control group, despite the absence of a pharmacist's intervention.

However, the methodologies used in QUMCIT and the Sutherland Project did not consider this parameter. Removing the attribution estimates from the model in the scenario analysis increased the estimated savings from reduced health resource usage

to an average of $115.18 per HMR, which is much closer than the baseline scenario to the estimated saving in this parameter of $159.91 predicted in the Sutherland project.[139] It seems reasonable to assume that, had attribution to the pharmacist been considered in QUMCIT and the Sutherland Project, then their estimates of savings to the healthcare system would be lower, and the estimate generated by the VALMER study may have been more comparable.

7.2.2.2 Study implications

7.2.2.2.1 Financial costs to the health system

The QUM Evaluation Program Projects suggested that the cost savings arising from HMRs can offset the cost of HMRs. Though it was not an objective of the VALMER study to directly evaluate this, it should be discussed in terms of as broader assessment of outcomes of HMRs in relation to financial costs to the health system. The VALMER study estimated that the average cost savings due to HMRs was $85.79 per HMR in the 12 months following the HMR, which was lower than the total cost of each HMR ($323.80). However, it cannot be concluded from this finding that HMRs do not result in benefits such that costs are totally offset due to the use of only the average cost savings across the sample of HMRs assessed in this study. Assessment of the HMRs in groups illustrates these limitations.

In the 60 HMRs assessed by the entire expert panel, there were 4 HMRs (7%) which were estimated to result in cost savings greater than $323.80, which completely offset the cost of the HMR. For this group of HMRs, there is little uncertainty that they generated more savings than the costs incurred by the health system. Amongst the remaining HMRs, it is possible that some proportion of them would have resulted in additional savings if costs resulting from ambulance and emergency department visits had been included. Whilst no Australian study has directly investigated whether HMRs reduce these costs, a prospective, controlled study conducted in the USA that investigated the effects of MMRs found a trend in reduced emergency department costs in the intervention group (P=0.054).[173] Despite this positive finding, it is debatable how much additional saving may have resulted if these costs were included in the VALMER study - a qualitative analysis of patients who had received HMRs found that 18% of them thought that they were more likely to attend an emergency department after the HMR, potentially due to greater awareness of ADEs.[15]

In addition to these HMRs, there may have been other cases where costs would have eventually been offset due to the commencement of preventative medications (as discussed previously), had the time horizon been greater than 12 months. The under-management of chronic medical conditions such as hypertension, hyperlipidaemia and osteoporosis is unlikely to result in short-term adverse health outcomes. Furthermore, improving the management of these conditions is unlikely to result in short-term (<12 months) health benefits. Nonetheless, the long-term economic benefits of improving the management of these conditions may be substantial, and it is most likely that restricting the time horizon in the VALMER study to 12 months limited the potential value of addressing these DRPs. In consideration of the limitations associated with the use of expert opinion, it was necessary to restrict the time horizon to 12 months in this study.

An issue that requires consideration when assessing if the benefits of HMRs offset the costs incurred by the program are the levels of remuneration to GPs and pharmacists. At the time of the VALMER study, GPs were reimbursed $140.20 per HMR (43% of the cost of the HMR). This is substantially higher than the levels used in the QUM Evaluation Program projects prior to the implementation of the HMR program, which were between $30 and $50 in most studies.[66, 86, 139, 142] This cost has increased substantially since 1997, especially relative to the reimbursement received by pharmacists ($100 in 1997 to $183.60 in 2008). The VALMER study found that accredited pharmacists' spend a median of 175 minutes undertaking each HMR, which equates to approximately $60 per hour for their involvement. Similar findings have been reported in previous studies of HMRs.[15, 203] No recent literature that investigated the time of GP involvement in the HMR process has been published.[xx] The scenario analysis in the VALMER study found that there was a 99% probability of cost-effectiveness if only the cost of the pharmacy component of the HMR professional service model was considered, with 16 HMRs (27%) estimated to offset costs in this scenario. Based on these data, it may be argued that a review of the level of GP

[xx] An evaluation of the GP component of the HMR program was undertaken for the Australian Government Department of Health and Ageing in 2005, and presumably this facet of the program was investigated at this time. However, as of July 2011, this report had not been released for public viewing

involvement and reimbursement is warranted, as managing this cost is essential if HMRs are to offset costs.

However, a substantial proportion of the HMRs were not likely to offset costs regardless of whether the time horizon was extended or if other costs were considered. For some of these HMRs, improved QOL was likely to have justified the expense of providing these patients HMRs, and the results of the cost-utility analysis are discussed below.

7.2.2.2.2 Utility analysis

Based on the expert assessment process, the VALMER study estimated that, on average, HMRs would have resulted in small but statistically significant improvements in QOL of 0.001 QALYs per patient. Although minor, it is important to recognise that the patients who were referred for the HMRs were suffering from multiple co-morbidities, and any improvement in health was likely to be appreciated by them.

The finding that a substantial proportion of the HMRs were estimated to result in little, if any, change to the patients' QOL was not unexpected as there is little evidence that medication reviews substantially improve this parameter. The only investigation into HMRs that has reported a substantial improvement in QOL was the flawed 2005 evaluation of the HMR program, which reported a gain of 0.119 QALYs per HMR.[15] In that study, 50 patients who had recently received HMRs completed the EQ-5D in recall mode (that is, they were asked to recall how they felt before the HMR, and compared to how they felt afterwards), a technique prone to recall bias. Of the QUM Evaluation Program Projects, only the St. George Canterbury Medico/ Pharmacy Project and the Domiciliary Medication Review Project directly examined QOL. Neither trial found that HMRs resulted in significant improvements in QOL.[66, 142] Similarly, most international studies of MMRs have found little QOL benefits resulted from the intervention, as discussed in Chapter One of this thesis.[23, 26, 47, 64]

Consideration of the DRPs identified in the HMRs again provides a potential explanation for the lack of substantial change in QOL. The most frequently identified DRP in the HMRs in the VALMER study was under-treated pain, and recommendations to introduce or intensify analgesics were common. Intuitively, such interventions

would be expected to improve QOL. However, given that the majority of patients in the study suffered from chronic pain conditions, such as osteoarthritis, the most common recommendation of increasing the dose or dose frequency of paracetamol may be unlikely to improve a patient's pain to a point that significant improvements in QOL will be apparent.[275] Commencing more potent analgesics such as opioids may improve pain, but adversely affect QOL in other ways, such as by causing adverse effects including constipation or sedation.[276] Additionally, there were many recommendations made to replace non-steroidal anti-inflammatory drugs with regular paracetamol, which is somewhat less efficacious in managing osteoarthritis pain.[277] In regards to the potential ADEs resolved by the HMRs in the study, those most frequently identified were relatively minor. The most common was cough resulting from ACE inhibitors, followed by muscle pain associated with statins. Resolving either issue was unlikely to substantially improve QOL for most patients.

An important finding of the VALMER study was that the HMRs were estimated to slightly worsen QOL in 20% of patients. Based on the results of previous MMR research, it was not unexpected that there were some HMRs that would potentially result in negative outcomes. However, the proportion of HMRs in which a detrimental effect on QOL was predicted to occur was somewhat higher than previous studies. In the Domiciliary Medication Review Project, 3.7% of the pharmacists' recommendations were reported to result in negative outcomes.[66] Similarly, between 5% and 10% of interventions in the Sutherland project were forecast to worsen DRPs,[139] as were 2.4% of the interventions in QUMCIT.[86] There are two potential reasons for these differences. Firstly, as discussed previously, the comparatively high proportion of medical practitioners in the expert panel may have resulted in a greater focus on detrimental outcomes than benefits. It is possible that if the proportions of pharmacists and medical practitioners in the expert panel used in the VALMER study were comparable to earlier studies, then the proportion of HMRs resulting in detrimental effects may have been similar to their findings.

Another possible explanation relates to the quality of the HMRs that were analysed. If the HMRs were of poor clinical quality, then it is likely that their benefits would be minimal or that detrimental effects may have occurred. Whilst the quality of the recommendations made by the pharmacists in this study was not directly assessed, there is some evidence that a high proportion of poor quality HMRs was unlikely to

have accounted for this finding. Given the large number of pharmacists who participated in the study, and that each of them had passed the relatively rigorous AACP accreditation process, it is unlikely that there would have been a large number of poor HMRs. Additionally, and more importantly, the high proportion of the pharmacists' recommendations that were implemented following the HMR implied that the GPs generally considered the pharmacist's findings relevant. Furthermore, in the scenario tested in the sensitivity analysis whereby the HMRs were valued had every recommendation been implemented, the QOL benefits of the HMRs was increased. Implicit in this finding is that the changes resulting from the pharmacists' recommendations were generally reasonable. Finally, a recent study by Castelino *et al*. reported that 94% of recommendations made by pharmacists in HMR reports were consistent with Australian guidelines.[55] In consideration of this, it seems likely that the comparatively high proportion of HMRs that would potentially worsen QOL did not result from poor quality HMRs.

Comments made by two of the expert assessors provide an alternative explanation. These experts suggested that, whilst clinical guidelines may recommend certain treatment standards, there is a need for pharmacists to ensure that the focus of HMRs remains centred on the patient at all times. One assessor commented,

> *"Too often the pharmacist did not seem to consider the potential impact on the patient, especially (with respect to) QOL issues…medication reviews must be patient centred - otherwise they are of no value to the patient nor GP. There were a lot of theoretical recommendations, which may be of some value but, largely, tell the GP to "suck eggs"."*
>
> -Pharmacist

Another expert indicated that there was an over-reliance on guidelines which do not consider the patient's co-morbidities or therapeutic objectives:

> *"Many of these patients were elderly and intensification of treatment might tick the box but might not meet the patient's goals. Patients do not always want to be treated according to the guidelines as different people place different value on different outcomes."*
>
> -Specialist physician

A similar comment was made by another expert:

> *"Deviations from vascular guidelines re antiplatelet and statin therapy were identified and should be considered but… if he were my patient, it would be about the time that I'd be discussing progressive withdrawal of multiple of these agents as risks rise and benefits decline."*
>
> -Specialist physician

Based on these comments, it is apparent that there may be an opportunity to optimise the QOL outcomes of HMRs by improving the skills of accredited pharmacists in interpreting and applying clinical guidelines to individual patients. However, this may prove to be challenging as there is limited literature regarding effective strategies to develop these skills.[278] Nonetheless, the results of the VALMER study indicate that investigating this potential may be highly worthwhile to improve the cost-effectiveness of HMRs.

7.2.2.2.3 Cost-utility analysis

The VALMER study found that the ICER for HMRs was $177 566 per QALY in the baseline ("best guess") scenario, and PSA identified that there was a 22% probability of cost-effectiveness using the WHO threshold of $150 000 per QALY. However, this finding cannot simply be considered as evidence that all HMRs are not cost-effective and funding for the HMR program should be reviewed. In contrast, these results should be interpreted in consideration of the scenario analysis, the outcomes of individual HMRs, and the limitations of the study to draw appropriate conclusions.

Firstly, of the numerous scenarios tested, the baseline scenario was one of the most conservative as the outcomes of the HMRs were discounted by the attribution and

uptake components of the model. The ICERs in the scenario analysis ranged from $89 210 (best case) to $225 462 (worst case) per QALY gained, with the ICER being below the threshold of $150 000 in all but the worst case scenario. More importantly, these are average figures, indicating that there were some HMRs where the ICER was below the threshold level and some were not. As mentioned in the earlier part of this discussion, if emergency department costs and ambulatory costs were included, or the study time horizon were extended, then the average saving was likely to have been increased and the average ICER in the baseline scenario may have satisfied the WHO threshold level.

However, the results of this facet of the study draws attention to the fact that many HMRs are not cost-effective, and this is likely to remain true even after inclusion of emergency department and ambulatory costs savings, and costs savings subsequent to the resolution of any service delivery issues. This resulted from minimal savings or QOL improvements occurring in a substantial number of the HMRs. This finding was not unexpected as it has been reported in several previous Australian and international studies of MMRs. For example, in QUMCIT, whilst all patients were satisfied with the service, 83.3% of them reported no change to their health.[86] More recently, in a qualitative study of the benefits and barriers of HMRs, several HMR recipients perceived that they had no need for the service.[279] In the HOMER study, it was reported that the pharmacists who undertook the MMRs felt that the visits were unlikely to be useful in 27% of patients.[155] In consideration of these findings, and those of the VALMER study, it is clearly apparent that there is a need to improve the proportion of HMRs that result in substantial cost savings or improved QOL. Based on this conclusion, a question which intuitively follows is, "*Which factors determine whether or not a HMR will be cost-effective?*". An analysis of the factors that potentially influenced the cost-effectiveness of the HMRs in the VALMER study is presented in the next chapter.

7.3 Limitations

The practicalities involved in undertaking the VALMER study resulted in a number of limitations which may have impacted upon its findings, and must be considered when interpreting the findings of the study. These limitations arose from aspects of the study's design and unforseen methodological issues, as discussed below.

7.3.1 Study design

7.3.1.1 Data collection

The first limitation resulted from the pharmacists who performed the HMRs being responsible for submitting them for the study. Upon enrolling in the study, pharmacists were asked to submit details of the next five HMRs that they performed. Despite the advertised requests for participation explicitly stating that no selection of HMRs should occur, the possibility that pharmacists may have submitted HMRs which they believed were of greater "value" than other HMRs they undertake cannot be ignored. Additionally, as the pharmacists first enrolled in the study then undertook the HMRs which they knew would be scrutinised, they may have taken more care when performing them. However, as the estimated average value of the HMRs was quite low, it seems unlikely that a substantial amount of selection of HMRs occurred. Additionally, the number and type of DRPs documented in the HMRs was consistent with the findings of previous HMR research, which further implies that selection of HMRs was unlikely to have substantially affected the validity of the VALMER study's findings.

A second possible limitation relates to the collection of the outcomes data. The pharmacist who performed the HMR was responsible for contacting the GP to obtain this data - the GP may have indicated that they accepted more recommendations than they did in reality. In the VALMER study, 82% of the DRPs were found to have been addressed in some way as a result of the HMR. In previous studies, the reported proportion of GP acceptance of recommendations made by pharmacists in HMRs varied from 38%[280] to 90%,[27] and the proportion in the VALMER study falls within these bounds. In addition, the largest study of HMRs to date reported that 81% of the identified DRPs were "resolved, well managed or improving",[126] and the VALMER study findings are not dissimilar to this figure.

7.3.1.2 Methodological limitations

A major limitation of the study resulted from the use of expert opinion to model the outcomes of the HMRs. By utilising expert opinion, the level of evidence provided by the study is intrinsically lower than if a controlled study design had been used.[205] This limitation cannot be overcome; however, numerous factors were considered when

designing the study to minimise confounding due to it. Firstly, the technique used to develop the estimates of the outcomes of the HMRs utilised a methodological framework that had been extensively developed in two previous studies.[191, 204, 281] This framework has been described as overcoming several key issues that may have adversely affected the validity of previous studies that used expert opinion to estimate the outcomes of pharmacists' interventions, including HMRs.[191] With regards to the experts who participated in the study, the types of health professionals were aligned with the recommendations of previous studies.[143] Each expert was an active practitioner and had extensive experience in managing patients similar to those reviewed in the HMRs. Most of the experts were involved in managing such patients on a regular basis in their usual practice. Several of them also possessed experience as academics and educators, and claimed to be very familiar with the medical literature relevant to the HMRs. It may therefore be argued that the limitations resulting from the use of expert opinion in the VALMER study were minimised, and the study's results are more robust than those of previous studies that also used expert opinion to assess the clinical and economic outcomes of HMRs.

However, by using Tenni's methodological framework,[191] a limitation that resulted from the concept of attribution to the pharmacist was introduced. Whilst it is clearly apparent that economic analyses of pharmacists' interventions in which there is the potential for other persons involved in a patient's care to perform the same intervention requires some attribution value, the values assigned by the experts were arbitrary estimates based purely on their experience and instinct. In the VALMER study, PSA and one-way sensitivity analysis was used to ensure that the uncertainty involving the attribution estimates was recognised, but it was not possible to completely overcome this limitation.

A second limitation that involved aspects of the economic modelling technique used for the study was that the consequence of *Death* was not a potential outcome that the experts could use in their assessment of the HMRs. Death would result in a total loss of utility and potentially substantial additional healthcare expenditure in affected patients. By not modelling death, it is possible that the VALMER study undervalued the benefits of HMRs that prevented lethal events. However, it may be argued that this limitation is unlikely to have greatly influenced the results as there is no evidence that MMRs reduce mortality, as reported in an international meta-analysis of 22 studies of

pharmacist-conducted medication reviews, including the Domiciliary Medication Review Project.[24]

A limitation that was more likely to influence the validity of the study's findings is the methodology's reliance on the accuracy of the estimates for each parameter in the consequences table. Although the parameter estimates were developed using a more rigorous methodology than Tenni's original consequences table, at best they can only be considered to be plausible and reasonable, and not reliable, validated, accurate estimates. Consequently, the economic outcomes of the HMRs in the VALMER study must only be considered to be broad estimates and not definitive figures.

In contrast to these limitations, which were unique to the VALMER study, other limitations were common to all studies in which expert opinion has been used. Implicit in the expert assessment process was that assumption that each assessor was able to accurately predict the potential outcomes of the DRPs identified in the HMRs given the information made available to them. The variation between the experts' opinions demonstrates that this was a difficult task - the results of the sensitivity analysis indicated a substantial difference in value between the baseline scenario and that where the *No consequence* data was excluded. It was attempted to partially address this limitation by providing the assessors with an option to not assess a case if they felt that they had insufficient information to do so. This option was used in only 0.016% of the HMR assessment, which may be considered to be evidence that that the assessors were relatively confident assessing the HMRs with the data available.

It is possible that the use of systematic reviews and meta-analyses may have improved the robustness of some of the results. However, for many of the DRPs identified (and indeed the recommendations made to resolve them), studies in elderly patients with numerous co-morbidities, such as those reviewed in the HMRs in this study, are limited. Hence, given the broad range of issues identified in such a diverse group of patients, it is unlikely that using systematic reviews as a primary source for estimating changes in risks resulting from the HMRs was either feasible or likely to substantially improve the robustness of the results.

A further limitation that resulted from the economic model used in the VALMER study is that no follow-up data, other than that collected by the reviewing pharmacist

shortly after the completion of the HMR, was analysed. As previously discussed, many of the pharmacists' recommendations required the GP *and* patient's acceptance for the recommendation to be implemented. The most accurate source of outcomes data would have been obtained from the final medication management plan. However, over 95% of the outcomes data was obtained by the reviewing pharmacist using the study's outcomes data form (Appendix III) and not the management plan, which may have documented only the GP's acceptance of the recommendation, and not the true outcome of the intervention (i.e. whether the patient agreed).

It was assumed that any changes to a patient's drug therapy that resulted from the HMR would have been sustained for the subsequent 12 months, which may not have been the case. Patients may have changed or discontinued medications several times throughout the following year. Whilst this limitation theoretically could have been overcome by asking the experts to predict the likelihood of each change being maintained, and what would have happened had the change not been maintained, this does not seem practical nor likely to produce robust results. Such an approach would introduce substantial further uncertainty, as it would most likely involve experts valuing a number of additional parameters primarily based on their instincts and experience, rather than literature. Neither would have conducting the study as a longitudinal design where drug regimen data were collected at several time points after the HMR, as this would have changed the potential probabilities of the clinical consequences and invalidated the experts' estimates of these. An additional limitation resulted from the assumptions regarding the use of "when-required" medications, which may have resulted in an overestimation of the increase in cost of drugs such as analgesics. Nonetheless, the findings regarding changes in drug costs were not dissimilar to those of QUMCIT and the Domiciliary Medication Review Project,[66, 86, 144] implying that this factor is unlikely to have significantly affected the validity of the results.

The lack of complete data for each patient resulted in another limitation to the VALMER study. The majority of information provided in HMR reports, and hence the focus of the economic analysis, related to clinical aspects of patient therapy. Advice or counselling provided by the pharmacist in the HMR interview was documented minimally, if at all. The findings therefore provided a conservative estimate of the potential value of this aspect of HMRs, which has been identified in other studies as a

major component of their benefits.[15, 30, 279] Furthermore, it was assumed that the first three DRPs identified in each HMR would be of the greatest significance to the patient's health, and therefore the most valuable. Subsequently, if the pharmacists who performed the HMRs did not prioritise the issues they identified, the model would have substantially discounted these valuable interventions. However, as the pharmacist survey found that 94% of participants *Always* or *Usually* prioritised the DRPs that they identified in the HMRs from most to least severe, it is unlikely that pharmacists not prioritising DRPs greatly affected the validity of the results.

This limitation was explored in the sensitivity analysis, whereby the DRPs that were not assessed by the experts were valued according to the average DRP value. To account for the potential that these DRPs were of lesser value than the assessed DRPs, the analysis was repeated whereby the average DRP value was discounted by 25%, 50% and 75%. In these scenarios, the probability of cost-effectiveness at a threshold of $150 000 ranged from 52% to 97%, which may be interpreted as evidence that the ICER calculated in the baseline scenario ($177 566 per QALY gained) was indeed affected by this limitation. Regardless, even in the best case scenario, whereby the average DRP value that was applied to the additional DRPs was not discounted, the analysis found a low probability (14%) of HMRs being highly cost-effective.

Another limitation resulting from this facet of the study is that it was the first three DRPs identified by the accredited pharmacist that were evaluated in the study, which may not have been the most clinically significant (or cost-effective). It was postulated that the accredited pharmacists stratified the DRPs from those they considered most important to least important. Whilst over 93% of the participating pharmacists stated that they "*Always*" or "*Usually*" did this, there was a proportion of pharmacists who did not. Furthermore, this approach assumed that the DRPs the pharmacists considered to be most important were the most clinically significant and/ or cost-effective. This may not have been the case, and hence the value of HMRs may be higher than the estimate generated in the study.

Related to this limitation is that 18 HMRs in which no DRPs were documented were excluded from the cost-utility analysis. This exclusion essentially assumed that these HMRs were of no value, and consequently the overall estimate of the savings resulting from HMRs developed in the study was exaggerated. However, as no DRPs were

documented in only 2.7% of the HMRs, it is unlikely that the validity of the findings was substantially influenced by this limitation. Furthermore, the extrapolation of the findings to HMRs Australia-wide (Section 6.3.4.1.5) accounted for this limitation, and only a minor difference was found when the HMRs with no DRPs were included in the analysis (cost of the program was $9.64 million versus $9.55 million).

Another limitation resulted from the perspective taken in the economic analysis. The VALMER study estimated the economic outcomes of HMRs from the perspective of the Australian government as a third party payer. Consequently, out-of-pocket costs to consumers were not considered, and may have limited the extent of both drug-cost savings and healthcare utilisation costs resulting from the HMRs. Conversely, a cost which was not accounted for in the model was the expense of additional regular monitoring which may have occurred subsequent to the HMR. As increased monitoring was the most common recommendation, the results of the VALMER study may be an underestimate of the changes in laboratory/ pathology costs associated with HMRs. However, it may be inferred from the results of the Domiciliary Medication Review Project that this would not have been the case.[66] In that study, increased monitoring was also the most frequently made recommendation, yet there was evidence of a reduction, rather than increase, in overall healthcare costs resulting from the medication review.

Finally, the economic analysis is based on the assumption that the 60 common HMRs were representative of all HMRs undertaken, which is unlikely to be the case. The comparisons between the sampled HMRs and the 661 HMRs submitted for the study identified that there were some differences between the patients in the number of drugs taken and their costs, and the number and types of DRPs identified. Had the planned methodology been followed, whereby 180 HMRs (27% of the HMRs in the study) were assessed by the experts, this limitation would have been less problematic. However, as a result of the discordance between the individual experts' opinions, the potential for this limitation to have affected the validity of the results of the economic evaluation must be acknowledged. This limitation, and others resulting from unforseen methodological issues in the study, is discussed in detail in the following section.

7.3.2 Methodological issues

In addition to the limitations resulting from the design of the VALMER study, several unforseen difficulties arose during the study which may have influenced the validity of its results. The most concerning of these was the extreme discordance observed between the experts in their predictions of the consequences that would be influenced as a result of the HMR. For example, in the assessment of the 60 HMRs assessed by every expert, there was 100% agreement between the experts, in terms of the consequences they selected, in only three of the 165 DRPs they assessed.

Based on the results of previous studies that used experts to predict the outcomes of pharmacists' interventions such as HMRs, it was not anticipated that there would be very high levels of agreement between the experts in the VALMER study. For example, four experts provided opinions on the HMRs in the Sutherland project, and poor agreement between them was reported as a limitation of that study.[139] Gisev *et al*. utilised a panel of four experts to evaluate the clinical impact and appropriateness of MMRs performed for clients of community mental health teams.[282] As shown in Figure 54, there was considerable discordance between the four experts with regards to the potential clinical impact of the MMRs.

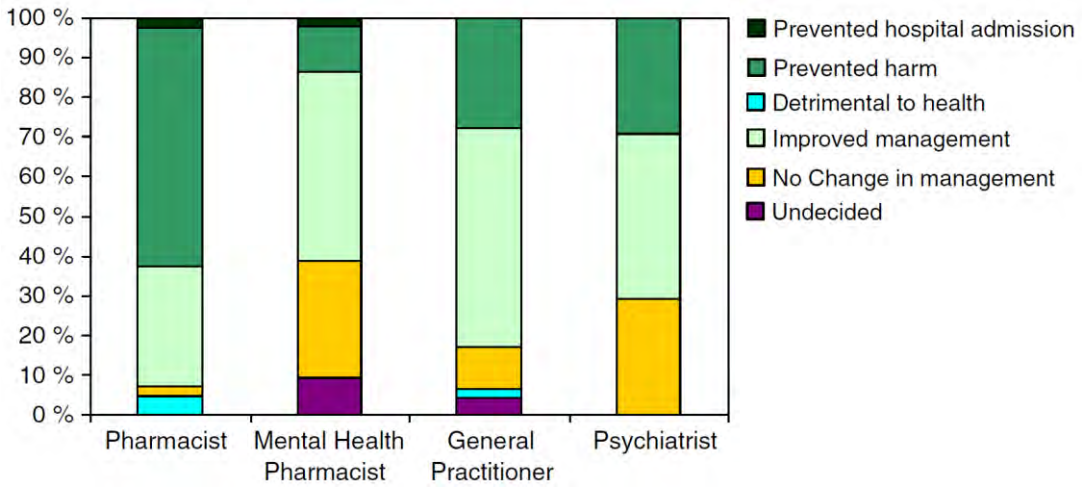

FIGURE 54 - ESTIMATED CLINICAL OUTCOMES OF MMRS UNDERTAKEN FOR CLIENTS OF COMMUNITY MENTAL HEALTH TEAMS. REPRODUCED FROM GISEV *ET AL.*[282]

In the study by Tenni in which the methodology used in the VALMER study was developed, there was limited investigation into the level of agreement between the experts in terms of the consequences selected.[204] Tenni compared only the costs calculated from each expert's estimates, rather than the consequences which resulted in these costs. In that study, it was stated that one of the expert's estimate of costs was higher than those of the other experts (shown in Figure 55), and that expert's estimates were excluded from the subsequent analysis. Despite using a similar approach to the VALMER study whereby each expert assessed a number of common DRPs and a series panel-specific DRPs, no consideration was given to differences between the panels and the results of the common and panel-specific interventions were analysed together.

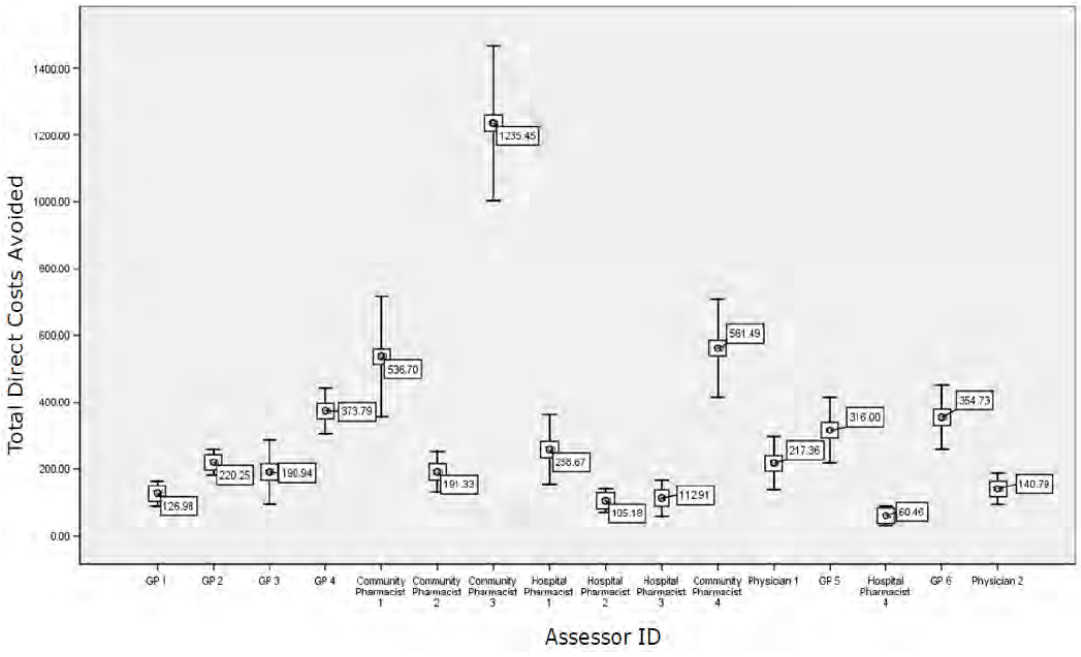

FIGURE 55 -AVERAGE TOTAL COST AVOIDANCE FOR ALL INTERVENTIONS BY DIFFERENT ASSESSORS IN STUDY BY TENNI. REPRODUCED FROM [204]

Figure 56 displays the equivalent data from the VALMER study (prepared from data presented in Table 112). It appears that each expert's average estimate, whilst varying

from approximately $100 in increased costs to $600 in savings, did not proportionally differ between the experts as much as in the study by Tenni.

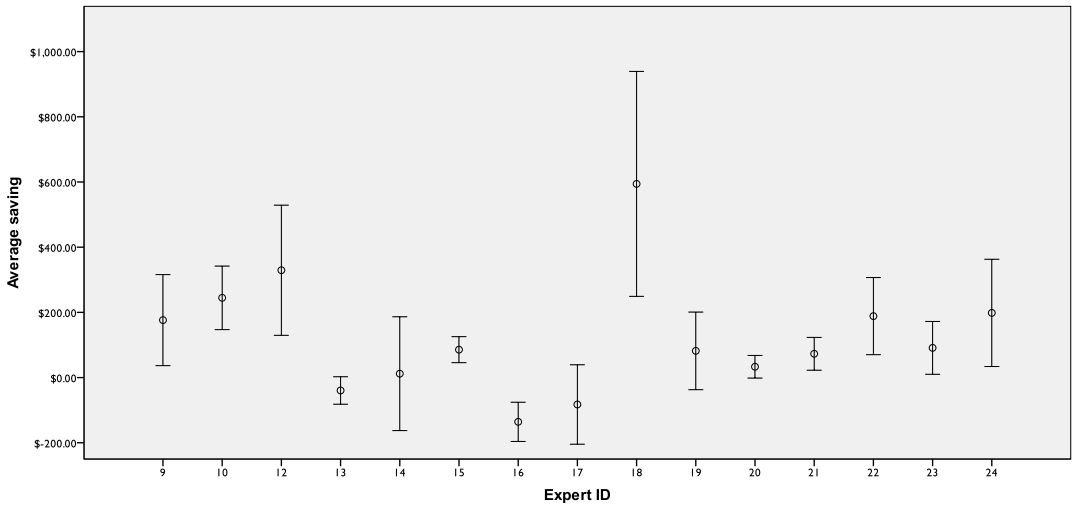

FIGURE 56 - INDIVIDUAL EXPERT RAW ESTIMATES OF AVERAGE HEALTHCARE COST CHANGES OCCURRING IN THE 60 HMRS ASSESSED BY EACH EXPERT IN THE VALMER STUDY. BARS REPRESENT 95% CONFIDENCE INTERVALS.

However, as shown in Table 113, the raw panel estimates of the cost and QOL changes resulting from the HMRs were not comparable, and therefore the number of HMRs that could be used in the full economic analysis was substantially smaller than planned.

Despite this issue, a major strength of the methodology employed in the VALMER study was that the differences between the opinions of the experts was recognised, and PSA was used in an attempt to demonstrate the potential range of outcomes based on these differences of opinion. Whilst it was not possible to totally overcome this limitation in the study, there are several recommendations that can be made for future research that uses the same methodology to minimise this limitation. The assessment process involved two stages- i) selection of consequences, and ii) assignment of probabilities to the selected consequences. Much of the discordance in the VALMER study arose from the experts selecting different consequences for the same intervention. This may have occurred for two major reasons. Firstly, it is

possible that there was a significant level of either research fatigue or difficulty in using the online HMR assessment system, and consequently the experts did not spend sufficient time in performing their assessment of the HMRs. Neither possibility can be verified as the system did not log time spent on each case, and the experts were not asked to comment on the user-friendliness of the system. However, several experts requested hard copies of the cases after commencing the assessment, and one expert provided their responses in a spread sheet and did not use the online system, which may imply that there were some issues with the system. Whilst the system used in the VALMER study was built by a professional website development company, it is possible that an improved user interface may have minimised this issue.

Secondly, there were 51 consequences to choose from, and the experts may have been unfamiliar with them. As a result, some experts may have selected the first few consequences in the list that they considered plausible, whereas other experts were more discerning in their choices and chose the consequences they thought most likely. This is supported by an expert, who commented at the conclusion of data collection,

> *"There were many more consequences that could have been entered but usually I didn't… usually I'd mentally discount a minor harm against a minor benefit and not enter either."*
>
> -Specialist physician

Prior to commencing their assessment of the HMRs, each expert was provided with a list of the consequences and their descriptive vignettes to familiarise them with the available consequences. However, the results of the VALMER study imply that this was insufficient, and a priority for future research that uses this methodology is to ensure some consistency between the experts in the consequences that they select.

There are several ways in which this may be achieved. Using a Delphi-type process involving sequential rounds of assessment by the experts may overcome this limitation to some degree, although this is likely to increase the total time taken for the expert assessment. An alternative solution was utilised by Peterson *et al*. in a study that used the same methodology as that used in the VALMER study to value clinical interventions performed in community pharmacies.[283] In that study, a

pharmacist researcher who prepared the cases for the expert assessment nominated what they felt to be the most important positive and negative consequences of the intervention, which were then reviewed by at least two other pharmacist researchers for agreement. The experts were asked to provide probability estimates for these consequences, but could also add any additional consequences they felt appropriate. Despite this additional step, there remained substantial differences between experts in their estimates of the savings resulting from the interventions (Figure 57). Nevertheless, the results of this study were considered to be sufficiently robust by the Australian government such that funding of AU$97 million was commenced for pharmacists to increase the number of clinical interventions provided in community pharmacies.[18]

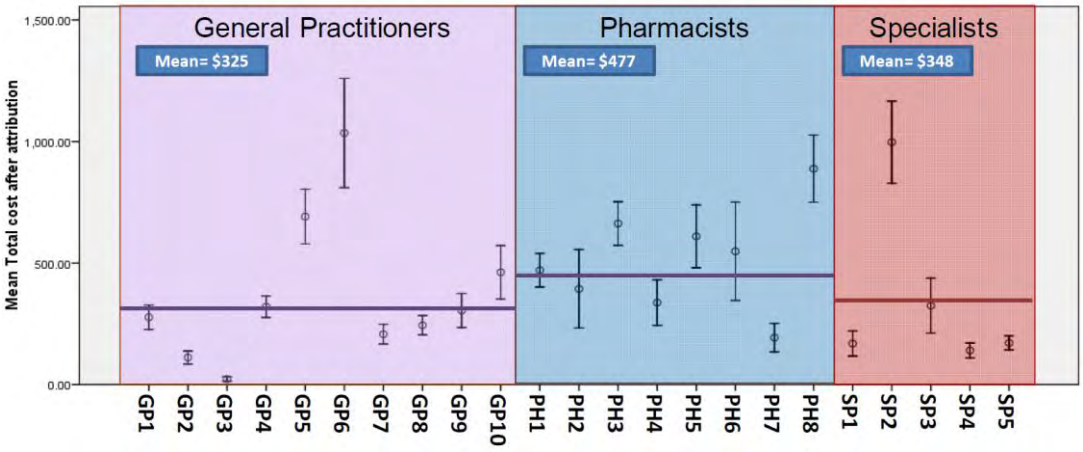

FIGURE 57 - MEAN SAVINGS ESTIMATES OF 23 EXPERT ASSESSORS IN STUDY BY PETERSON *ET AL*. REPRODUCED FROM[283]

Finally, it seems prudent to recommend avoiding splitting the interventions to be assessed into common and panel-specific interventions, if possible. Although this approach has been used in studies other than the VALMER study,[193, 204] the variability between experts may cause difficulty in analysing the results. Based on this finding of the VALMER study, the aforementioned study by Peterson *et al*., which was originally planned to involve assessment of common and panel-specific interventions, was modified so that each expert assessed the same set of cases.

7.4 Conclusions

The evaluation of HMRs undertaken in the VALMER study is one of the most comprehensive to date. The study characterised the patients referred for HMRs and the DRPs identified in them, and determined that HMRs may result in significant improvements in a number of clinical consequences. Despite the failure of the VALMER study to provide a definitive conclusion regarding the cost-effectiveness of HMRs under the current funding model, the study identified that some HMRs are likely to be highly cost-effective, and there is a need for research to focus on improving the targeting of HMRs to patients who may benefit from them the most. Furthermore, the results of aspects of the VALMER study have had significant implications for expanding professional services for which pharmacists receive remuneration from the Australian government.

Chapter 8 - Factors related to the cost-effectiveness of HMRs

8.1 Introduction

One of the most important findings of the VALMER study was that some HMRs are highly cost-effective; however, the proportion of these HMRs is too low for the HMR program, as currently structured, to be cost-effective. Consequently, there is a need to increase the proportion of HMRs performed that result in substantial savings or improved QOL, to improve the cost-effectiveness of the overall HMR program. In this chapter, an analysis of the factors that potentially influenced the cost-effectiveness of the HMRs in the VALMER study is presented, as these findings may have implications for further research into ways to improve the cost-effectiveness of the HMR program.

To date, no studies have directly investigated the factors that predict the cost-effectiveness of individual HMRs. However, some insight is provided by the results of previous research which has focused on patients with specific conditions. Several studies have identified that patients who receive HMRs post-hospital discharge are likely to benefit from them.[149, 284-286] Consequently, there is provision for developing a specific post-discharge HMR model in the most recent Community Pharmacy Agreement.[18] Stafford *et al*. recently reported that a home-based post-discharge warfarin management service adapted from the HMR program resulted in decreased rates of combined major and minor bleeding up to 90 days post-discharge compared to usual care (5.3% versus 14.7%; *P*=0.03).[287] There is also some evidence that HMRs may be of benefit to patients with heart failure, as some studies have associated HMRs with reductions in hospitalisation in these patients.[174, 285] However, it should be acknowledged that several studies of MMR models, other than HMR, did not find that the intervention reduced hospitalisations.[168, 288, 289]

As discussed in Chapter One of this thesis, the Australian guidelines for the provision of HMR services specify several factors to assist in identifying patients who may benefit most from the service.[290] These include polypharmacy, potential ADEs, taking medication of a narrow therapeutic index or requiring therapeutic monitoring, or

suspected compliance issues. However, the outcomes of HMRs in patients with and without these factors have not been investigated.

In addition to patient characteristics, it is possible that a number of factors related to the HMR service model may also influence the outcomes of HMRs. The VALMER study identified that there was a high degree of variability in the conduct of multiple aspects of the HMR process, including the information contained in the referrals to accredited pharmacists, the DRPs identified in the HMRs and the recommendations made to resolve them. With regard to the content of the HMR referral, there is no direct evidence that the quantity of information documented in referrals affects the outcomes of HMRs, although there is some literature that implies that this could be the case. In a US study, Warholak-Juarez *et al*. reported that the quality of pharmacists' clinical decisions in drug utilisation reviews were improved when more detailed patient information was available to them.[291] In an RCT of MMRs conducted for elderly patients in the UK, Krska *et al*. reported that 18% of DRPs detected by pharmacists required the use of medical notes.[47] De Smet *et al*. reviewed the literature pertaining to the process of conducting MMRs and concluded that medication reviewers may identify and evaluate certain types of DRPs only, or more readily, with access to medical records.[292] Additionally, poor quality communication between doctors has been associated with increased medical complaints and claims by patients, potentially due to negative patient outcomes.[293] Anecdotal evidence from accredited pharmacists (Appendix XXIV) supports the hypothesis that a lack of relevant information in a HMR referral may adversely influence the quality, and therefore the outcomes, of the HMR. It may therefore be argued that an investigation into the factors that potentially influenced the cost-effectiveness of the HMRs in the VALMER study must consider both patient characteristics and the level of information provided to the reviewing pharmacist.

Another potential influence on the outcomes of HMRs involves the characteristics of the accredited pharmacists who performed the HMRs. Although the majority of pharmacists undertaking HMRs are accredited with the AACP,[131, 132] the pharmacist survey in the VALMER study found substantial variation between them in factors such as HMR and workplace experience, participation in continuing education, and the time taken to complete HMRs. However, there is scant literature that has investigated the extent to which pharmacist characteristics may influence the outcomes of MMRs. One

of the few studies that investigated this was a review of pharmaceutical care interventions for patients with asthma, which identified that additional pharmacist training was associated with more favourable patient outcomes.[294]

In a study by Krska and Avery, two researchers identified DRPs from the notes of a sample of patients who received MMRs in a RCT in the UK.[59] These DRPs were compared to those documented by the pharmacists who performed the MMRs in the trial to identify the proportion of absent or inappropriate DRPs. The relationship between the pharmacists' characteristics and the proportion of DRPs not identified by them was then assessed. No relationship between the pharmacists' workplace experience, educational history or time since completion of their initial pharmacist-related qualification was identified. In contrast, in a retrospective analysis of HMRs, Stafford *et al*. reported that pharmacists who had completed their undergraduate pharmacy degree after 1980 identified a greater number of DRPs of high clinical significance than pharmacists who graduated prior to 1980 (0.7 more DRPs per review, 95% CI 0.2 to 1.2, $P<0.005$).[295]

In conclusion, it is possible that a number of factors, including patient characteristics, referral contents and pharmacist characteristics, may influence the outcomes and cost-effectiveness of HMRs. The aim of this sub-study was to explore potential relationships between these factors and the estimated cost-effectiveness of the HMRs in the VALMER study. Notably, the identification of significant relationships in this study does not imply causality, and can only be considered to provide insight into avenues for further research into improving the cost-effectiveness of HMRs and the HMR program.

8.2 Methods

The results of the baseline scenario cost-utility analysis of the 60 HMRs assessed by each expert in the VALMER study were used for this evaluation. This was because the estimates of costs and QOL effects resulting from these HMRs were likely to be more robust than the 120 HMRs assessed by the different panels, as discussed in Chapter 6. Whilst a number of scenarios analyses were investigated in Chapter 6, and therefore several datasets could have been used, the baseline scenario was considered to be the most conservative ("best guess"), and was appropriate to use for the analysis in this

chapter. The average cost per QALY gained for each HMR (ICER) was calculated, and the HMRs were investigated according to two different thresholds of cost-effectiveness in consideration of the limited number of HMRs used in the analysis:

- In the first analysis, the HMR was classed as either *Highly cost-effective* (if the average ICER was ≤$50 000) or *Not highly cost-effective* (if the HMR was estimated to result in lost QOL or the average ICER was ≥$50 000).
- In the second analysis, each HMR was classed as *Cost-effective* (if in the dominant quadrant or the ICER was ≤$150 000 or *Not cost-effective* (if the HMR was estimated to result in lost QOL or the ICER was ≥$150 000).

Given the lack of literature in the area, a broad range of factors were investigated for relationships with cost-effective HMRs. Three general types of factors were investigated, as follows:

- *Patient factors*: sex, age group, number of diagnosed conditions, monthly drug cost, number of regular medications, and taking a drug of specific interest (as discussed in Section 5.4.3.2);
- *Pharmacist factors*: sex, education history, employment history and experience, medication review experience, and medication review techniques; and
- *HMR process factors*: type of information documented in the HMR referral, and duration of patient interview.

The *Patient* and *HMR process factor* data were sourced from the HMR data submitted for the VALMER study. The results of the VALMER study pharmacist survey and the AACP accreditation/reaccreditation MCQ scores were used to investigate the *Pharmacist factors*. A summary of the factors, the data used for the analysis and the justification for the inclusion of these factors in the analysis, is shown in Table 134.

To account for the potential that a single pharmacist may have submitted more than one HMR, and that these pharmacists may have produced some HMRs that were cost-effective and some that were not, the analysis of the pharmacist factors necessitated an additional grouping of the data. Depending upon the threshold of cost-effectiveness ($50 000 or $150 000 per QALY gained), each pharmacist was classified as follows:

- in the first analysis, if at least one of the HMRs performed by a pharmacist was *Cost-effective*, then the pharmacist was classified as being *Capable of cost-effectiveness*, and
- in the second analysis, if at least one of the HMRs performed by a pharmacist was *Highly cost-effective*, then the pharmacist was classed as *Capable of high cost-effectiveness*.
- if no HMR performed by the pharmacist was *Cost-effective* or *Highly cost-effective*, then the pharmacist was classified as *Not capable of cost-effectiveness* and *Not capable of high cost-effectiveness* respectively.

Pearson χ^2 tests were used to identify relationships between HMRs and categorical factors, and Mann Whitney tests were used to investigate continuous variables, as all were non-parametrically distributed.

TABLE 134 - FACTORS INVESTIGATED FOR RELATIONSHIPS WITH COST-EFFECTIVENESS OF HMRS

FACTOR TYPE FACTOR	DATA SOURCE	DESCRIPTION AND RATIONALE
Patient factors		
Sex	HMR referral	Male or female; not investigated to date.
Age group	HMR referral	Grouped according to definitions frequently used in literature: <65 years (younger), 65 to 75 years (elderly), >75 years (very old).[296] Risk of medication misadventure reported to increase with age.[11]
Number of diagnosed medical conditions	HMR referral	Continuous variable; risk of medication misadventure reported to increase with increased co-morbidities.[260]
Number of regular medications	HMR referral	Continuous variable; risk of medication misadventure reported to increase with increased number of drugs.[259]
Monthly drug cost ($)	Calculated in VALMER study	Continuous variable; drug costs reported to be useful to identify patients that may benefit from MMRs.[58]
Drug/group of specific interest	HMR referral	Drugs of narrow therapeutic index or frequently involved in DRPs as outlined in section 5.4.3.2 : ACE inhibitors and angiotensin 2 receptor antagonists, antiplatelet agents, digoxin, diuretics, HMG-CoA reductase inhibitors, NSAIDs, paracetamol, proton pump inhibitors, and warfarin.
Pharmacist factors		
Sex	VALMER pharmacist survey	Male or female; not investigated to date.
Postgraduate qualification	VALMER pharmacist survey	Yes or no; additional training associated with improved processes and outcomes of pharmaceutical care and medication-review.[294, 297]
Medication review as primary occupation	VALMER pharmacist survey	Yes or no; not investigated to date.
Hospital pharmacy experience	VALMER pharmacist survey	Yes or no; suggested that hospitals provide the most appropriate environment for training consultant pharmacists.[298]
Frequency of discussion about HMRs with referring GPs	VALMER pharmacist survey	Grouped according to discussion occurring in <50% or ≥50% of HMRs. Not investigated to date; suggested that interaction with other healthcare professionals develops an appreciation of clinical decision-making.[298]
Uses medication review software for HMRs	VALMER pharmacist survey	Yes or no; not investigated to date.
Number of years since undergraduate degree completed	VALMER pharmacist survey	Continuous variable; reported that more recent graduates identified a greater number of DRPs of high clinical significance than earlier graduates.[295]

FACTOR TYPE FACTOR	DATA SOURCE	DESCRIPTION AND RATIONALE
HMR experience	VALMER pharmacist survey	Continuous variables; number of years medication review accredited, number of years performing HMRs, number of HMRs completed recently and in total. Not investigated to date.
Hours of continuing education in previous year	VALMER pharmacist survey	Continuous variable; continuing education in medical practitioners has been associated with improvements in several clinical outcomes such as arthritis pain, depression, general health and function, reduced hospitalisations and reduced length of hospital admissions.[299]
Accreditation / reaccreditation examination performance	AACP examination score	Continuous variable; not investigated to date.
HMR process factors		
Reason/s for HMR referral	HMR referral	Grouped as either *Clear* or *Not stated/unclear*; not investigated to date.
Pathology and lab results	HMR referral	Grouped as either *Irrelevant, limited or absent*, or *Recent and potentially relevant* according to criteria in Table 97. Reported that access to medical records improves DRP identification.[59, 292]
Medical history	HMR referral	Grouped as either *Detailed*, or *Minimal* according to criteria in Table 97. Reported that access to medical records improves DRP identification. [59, 292]
Time taken to perform HMR	Provided by participating pharmacist	Continuous variables; interview time and total HMR time not investigated to date.

8.3 Results

Of the 60 HMRs included in this analysis, 10 HMRs (17%) were *Highly cost-effective* as their average ICER was ≤$50 000 per QALY gained. At the threshold of cost-effectiveness of $150 000 per QALY gained, 21 HMRs (35%) were classified as C*ost-effective*.

8.3.1 Patient factors

The relationships between the categorical patient factors and cost-effectiveness or high cost-effectiveness of HMRs are shown in Table 135. No significant relationship between patient sex and cost-effectiveness or high cost-effectiveness was identified. A trend towards a greater proportion of highly cost-effective HMRs in older patients was observed (*P*=0.08), although the numbers of HMRs were small and the trend was not apparent in the cost-effective HMR analysis (*P*=0.32).

TABLE 135 - RESULTS OF INVESTIGATIONS INTO RELATIONSHIPS BETWEEN POTENTIAL PATIENT-RELATED DETERMINANTS OF COST-EFFECTIVENESS OF HMRS INVOLVING PATIENT CHARACTERISTICS

CHARACTERISTIC	NUMBER (% OF TOTAL) OF HMRS				
	TOTAL	HIGHLY COST-EFFECTIVE	TEST RESULT	COST-EFFECTIVE	TEST RESULT
SEX					
Male	17 (28.3)	4 (23.5)	$\chi^2(1)=0.804$ *P*=0.45	7 (41.2)	$\chi^2(1)=0.528$ *P*=0.56
Female	43 (71.7)	6 (14.0)		14 (32.6)	
AGE GROUP					
< 65 years	9 (15)	0 (0.0)	$\chi^2(2)=5.113$ *P*=0.08	2 (22.2)	$\chi^2(2)=2.299$ *P*=0.32
65 to 75 years	16 (26.7)	1 (6.3)		15 (93.8)	
> 75 years	35 (58.3)	9 (25.7)		4 (11.4)	
TOTAL	**60 (100)**	10 (16.7)		21 (35.0)	

The results of the analysis of the continuous variables and cost-effective HMRs are shown in Table 136. No significant relationship between any of the factors investigated and cost-effectiveness was observed.

TABLE 136 - RESULTS OF INVESTIGATIONS INTO RELATIONSHIPS BETWEEN POTENTIAL PATIENT-RELATED DETERMINANTS OF COST-EFFECTIVE HMRS - CONTINUOUS VARIABLES

PARAMETER	COST-EFFECTIVE (N=21)		NOT COST-EFFECTIVE (N=39)		TEST RESULT
	MEDIAN	IQR	MEDIAN	IQR	
Number of diagnosed medical conditions	8	5	8	6	*U*=381.5, *Z*=-0.412 *P*=0.68
Number of regular medications	11	4	10	6	*U*=408.5, *Z*=-0.016 *P*=0.99
Monthly drug cost ($)	265.53	141.23	241.22	207.11	*U*=367, *Z*=-0.659 *P*=0.51

Similarly, no significant relationship between any of the continuous variables investigated and high cost-effectiveness was identified (Table 137).

TABLE 137 - RESULTS OF INVESTIGATIONS INTO RELATIONSHIPS BETWEEN POTENTIAL PATIENT-RELATED DETERMINANTS OF HIGHLY COST-EFFECTIVE HMRS - CONTINUOUS VARIABLES

PARAMETER	HIGHLY COST-EFFECTIVE (N=10)		NOT HIGHLY COST-EFFECTIVE (N=50)		TEST RESULT
	MEDIAN	IQR	MEDIAN	IQR	
Number of diagnosed medical conditions	9	4	8	6	*U*=197.5, *Z*=-0.664, *P*=0.51
Number of regular medications	12	6	10	5	*U*=215, *Z*=-0.301, *P*=0.76
Monthly drug cost ($)	268.81	45.68	249.84	198.66	*U*=209, *Z*=-0.424, *P*=0.67

The relationship between patients taking a drug of specific interest and the cost-effectiveness of the HMRs is shown in Table 138. There was no statistically significant relationship observed between any single drug/group of specific interest and HMR cost-effectiveness.

TABLE 138 - RESULTS OF INVESTIGATIONS INTO RELATIONSHIPS BETWEEN POTENTIAL PATIENT-RELATED DETERMINANTS OF COST-EFFECTIVENESS OF HMRS INVOLVING DRUGS OF SPECIFIC INTEREST

DRUG/GROUP OF SPECIFIC INTEREST	NUMBER (% OF TOTAL) OF HMRS				
	PATIENTS TAKING	HIGHLY COST-EFFECTIVE	TEST RESULT	COST-EFFECTIVE	TEST RESULT
ACE inhibitors and angiotensin 2 receptor antagonists	47 (78.3)	7 (14.9)	$\chi^2(1)=0.491$ $P=0.67$	15 (31.9)	$\chi^2(1)=0.908$ $P=0.35$
Antiplatelet agents	31 (51.7)	7 (22.6)	$\chi^2(1)=1.615$ $P=0.30$	12 (38.7)	$\chi^2(1)=0.388$ $P=0.59$
Digoxin	12 (20.0)	2 (16.7)	$\chi^2(1)=0.000$ $P=1.00$	3 (25.0)	$\chi^2(1)=0.659$ $P=0.51$
Diuretics	18 (30.0)	3 (16.7)	$\chi^2(1)=0.000$ $P=1.00$	5 (27.8)	$\chi^2(1)=0.590$ $P=0.56$
HMG-CoA reductase inhibitors	37 (61.7)	6 (16.2)	$\chi^2(1)=0.014$ $P=1.00$	14 (37.8)	$\chi^2(1)=0.342$ $P=0.59$
Non-steroidal anti-inflammatory drugs	24 (40.0)	3 (12.5)	$\chi^2(1)=0.500$ $P=0.72$	9 (37.5)	$\chi^2(1)=0.110$ $P=0.79$
Paracetamol	41 (68.3)	8 (19.5)	$\chi^2(1)=0.755$ $P=0.48$	14 (34.1)	$\chi^2(1)=0.041$ $P=1.00$
Proton pump inhibitors	37 (61.7)	4 (10.8)	$\chi^2(1)=2.383$ $P=0.16$	11 (29.7)	$\chi^2(1)=1.178$ $P=0.40$
Warfarin	10 (16.7)	0 (0.0)	$\chi^2(1)=2.40$ $P=0.19$	2 (20.0)	$\chi^2(1)=1.187$ $P=0.47$

8.3.2 Pharmacist factors

The 60 HMRs in the dataset were performed by 47 different pharmacists; 35 pharmacists had performed a single HMR, 11 pharmacists two HMRs and one pharmacist had performed three HMRs. Of these 47 pharmacists, survey responses were available for 38 of them, and AACP accreditation/reaccreditation MCQ scores were available for 32 of them.

The relationships between the categorical pharmacist factors and cost-effectiveness or high cost-effectiveness of HMRs are shown in Table 139. No significant relationship between any of the factors investigated and cost-effectiveness or high cost-effectiveness was identified.

TABLE 139 - RESULTS OF INVESTIGATIONS INTO RELATIONSHIPS BETWEEN POTENTIAL PHARMACIST-RELATED DETERMINANTS OF COST-EFFECTIVENESS OF HMRS - CATEGORICAL VARIABLES

	NUMBER (% OF TOTAL) OF PHARMACISTS				
	TOTAL	HIGHLY COST-EFFECTIVE	TEST RESULT	COST-EFFECTIVE	TEST RESULT
SEX					
Male	9 (23.7)	3 (33.3)	$\chi^2(1)=0.607$	4 (44.4)	$\chi^2(1)=0.122$
Female	29 (76.3)	6 (20.7)	*P*=0.65	11 (37.9)	*P*=1.00
POSTGRADUATE QUALIFICATION					
No	26 (68.4)	7 (26.9)	$\chi^2(1)=0.478$	12 (46.2)	$\chi^2(1)=1.538$
Yes	12 (31.6)	2 (16.7)	*P*=0.69	3 (25.0)	*P*=0.29
MEDICATION REVIEW AS PRIMARY OCCUPATION					
No	25 (65.8)	5 (20.0)	$\chi^2(1)=0.549$	8 (32.0)	$\chi^2(1)=1.708$
Yes	13 (34.2)	4 (30.8)	*P*=0.69	7 (53.8)	*P*=0.29
HOSPITAL PHARMACY EXPERIENCE					
No	15 (39.5)	4 (26.7)	$\chi^2(1)=0.122$	7 (46.7)	$\chi^2(1)=0.537$
Yes	23 (60.5)	5 (21.7)	*P*=1.00	8 (34.8)	*P*=0.51
FREQUENCY OF DISCUSSION ABOUT HMRS WITH REFERRING GP					
≥50% of HMRs	4 (10.5)	0 (0.0)	$\chi^2(1)=1.387$	1 (25.0)	$\chi^2(1)=0.392$
<50% of HMRs	34 (89.5)	9 (26.5)	*P*=0.55	14 (41.2)	*P*=1.00
USES MEDICATION REVIEW SOFTWARE FOR HMRS					
No	29 (76.3)	7 (24.1)	$\chi^2(1)=0.014$	11 (37.9)	$\chi^2(1)=0.122$
Yes	9 (23.7)	2 (22.2)	*P*=1.00	4 (44.4)	*P*=1.00
TOTAL	**38 (100)**	**9 (23.7)**		**15 (39.5)**	

Table 140 shows the results of the analysis of the continuous pharmacist-related variables and cost-effective HMRs. Two factors were found to relate to the cost-effectiveness of the HMRs - in the cost-effective HMRs, pharmacists had undertaken a greater number of hours of continuing education in the previous year (*P*=0.006), and had performed a greater total number of HMRs (*P*=0.041).

TABLE 140 - RESULTS OF INVESTIGATIONS INTO RELATIONSHIPS BETWEEN POTENTIAL PHARMACIST-RELATED DETERMINANTS OF COST-EFFECTIVE HMRS - CONTINUOUS VARIABLES

PARAMETER	COST-EFFECTIVE (N=15)		NOT COST-EFFECTIVE (N=23)		TEST RESULT
	Median	IQR	Median	IQR	
Number of years since undergraduate degree completed	24*	14	25	17	*U*=169.5, *Z*=0.660 *P*=0.515
Number of years medication review accredited	6	3	6	8	*U*=200, *Z*=0.588 *P*=0.578
Number of years since first HMR	6	3	5	5	*U*=216, *Z*=1.316 *P*=0.202
Number of HMRs ever completed	**600**	**900**	**250**	**400**	***U*=104.5, *Z*=-2.034 *P*=0.041**
Number of HMRs completed in 2008	138	356	80	110	*U*=131, *Z*=-1.240 *P*=0.224
Hours of continuing education in previous year	**99**	**100**	**50**	**35**	***U*=81.5, *Z*=-2.729 *P*=0.006**
Accreditation / reaccreditation examination score (/50)	43	5	42.5**	6	*U*=119.5, *Z*=-0.563 *P*=0.580

*n=13; **n=18

As two factors were identified in this analysis, the appropriateness of further investigation using multiple logistic regression was considered at this point. However, this was thought to be inappropriate as the sample size for the analysis was much smaller than the minimum recommended, and there would have been a high likelihood that the results of such an analysis would have been confounded.[300]

Consequently, a simple correlation analysis between the number of HMRs ever completed and the hours of continuing education in previous year was performed. The Pearson product-moment correlation indicated that there was minimal correlation between the two variables (r=-0.148, n=38, P=0.38) in all pharmacists. In the pharmacists who had performed cost-effective HMRs, there was significant moderate negative correlation between the two variables (r=-0.518, n=15, P=0.048), but this was not observed in the pharmacists who had not performed cost-effective HMRs (r=-0.107, n=23, P=0.63).

The results of the analysis of the continuous pharmacist-related variables and highly cost-effective HMRs are shown in Table 141. In contrast to the results of the previous analysis, a relationship between only the number of hours of continuing education in the previous year and highly cost-effective HMRs was identified, in which the pharmacists who had performed highly cost-effective HMRs had undertaken a

significantly greater amount of continuing education than the pharmacists who had not performed highly cost-effective HMRs (*P*=0.001).

TABLE 141 - RESULTS OF INVESTIGATIONS INTO RELATIONSHIPS BETWEEN POTENTIAL PHARMACIST-RELATED DETERMINANTS OF HIGHLY COST-EFFECTIVE HMRS - CONTINUOUS VARIABLES

PARAMETER	HIGHLY COST-EFFECTIVE (N=9)		NOT HIGHLY COST-EFFECTIVE (N=29)		TEST RESULT
	Median	IQR	Median	IQR	
Number of years since undergraduate degree completed	24.5*	17	22.5**	17	*U*=123.5, *Z*=0.438 *P*=0.668
Number of years medication review accredited	6	4	6	4	*U*=107, *Z*=-0.822 *P*=0.436
Number of years since first HMR	6	5	5	3	*U*=98, *Z*=-1.131 *P*=0.277
Number of HMRs ever completed	500	720	300	575	*U*=93, *Z*=-1.290 *P*=0.208
Number of HMRs completed in 2008	75	230	90	157	*U*=117, *Z*=-0.464 *P*=0.661
Hours of continuing education in previous year	**130**	**81**	**50**	**47**	***U*=41, *Z*=-3.085 *P*=0.001**
Accreditation / reaccreditation examination score (/50)	42	4	43.5***	6	*U*=144.5, *Z*=1.483 *P*=0.142

*n=8; **n=28; *** n=24

8.3.3 Process factors

The relationships between the categorical process factors and cost-effectiveness or high cost-effectiveness of HMRs are shown in Table 142. A relationship between the level of completeness of medical history in the referral and cost-effective HMRs was identified, where a greater proportion of HMRs with minimal medical history in the referrals were more cost-effective compared to HMRs with detailed medical history (*P*=0.026). In the analysis of the referrals for the highly cost-effective HMRs, a greater proportion contained potentially useful pathology and laboratory results compared to the HMRs that were not highly cost-effective (*P*=0.033), although the number of HMRs in this analysis was again small. Interestingly, there was no clear reason for the HMR referral stated for each HMR that was highly cost-effective.

TABLE 142 - RESULTS OF INVESTIGATIONS INTO RELATIONSHIPS BETWEEN POTENTIAL REFERRAL-RELATED DETERMINANTS OF COST-EFFECTIVENESS OF HMRS

CHARACTERISTIC	NUMBER (% OF TOTAL) OF HMRS				
	TOTAL	HIGHLY COST-EFFECTIVE	TEST RESULT	COST-EFFECTIVE	TEST RESULT
REASON/S FOR REFERRAL					
Clear	19 (31.7)	0 (0.0)	**$\chi^2(1)=5.561$ *P*=0.02**	5 (26.3)	$\chi^2(1)=0.922$ *P*=0.39
Not stated	41 (68.3)	10 (24.4)		16 (39.0)	
PATHOLOGY AND LABORATORY RESULTS					
Irrelevant, limited or absent	26 (43.3)	1 (3.8)	**$\chi^2(2)=5.430$ *P*=0.03**	8 (30.8)	$\chi^2(2)=0.361$ *P*=0.59
Recent and potentially relevant	34 (56.7)	9 (26.5)		13 (38.2)	
MEDICAL HISTORY					
Detailed	24 (40.0)	3 (12.5)	$\chi^2(2)=0.500$ *P*=0.72	4 (16.7)	**$\chi^2(2)=5.910$ *P*=0.03**
Minimal	26 (60.0)	7 (26.9)		17 (65.4)	
TOTAL	**60 (100)**	**10 (16.7)**		**21 (35.0)**	

The results of the analysis of the relationship between the time taken to perform the HMRs and their cost-effectiveness are shown in Table 143. No significant relationship between either the time taken to perform the HMR interview, or the total HMR time, and cost-effectiveness was observed.

TABLE 143 - RESULTS OF INVESTIGATIONS INTO RELATIONSHIP BETWEEN INTERVIEW OR TOTAL HMR TIME AND COST-EFFECTIVENESS AT A THRESHOLD OF $150 000 PER QALY GAINED

PARAMETER	HIGHLY COST-EFFECTIVE HMRS (N=21)		NOT HIGHLY COST-EFFECTIVE HMRS (N=39)		TEST RESULT
	MEDIAN	IQR	MEDIAN	IQR	
Interview	60	15	60	20	*U*=344, *Z*=-0.132 *P*=0.89
Total HMR	220	130	195	135	*U*=330.5, *Z*=-0.364 *P*=0.72

Similarly, neither were there significant relationships between the highly cost-effective HMRs and the time taken to perform the HMR interview or the total HMR time (Table 144).

TABLE 144 - RESULTS OF INVESTIGATIONS INTO RELATIONSHIP BETWEEN INTERVIEW OR TOTAL HMR TIME AND COST-EFFECTIVENESS AT A THRESHOLD OF $150 000 PER QALY GAINED

PARAMETER	HIGHLY COST-EFFECTIVE HMRS (N=10)		NOT HIGHLY COST-EFFECTIVE HMRS (N=50)		TEST RESULT
	MEDIAN	IQR	MEDIAN	IQR	
Interview	60	15	60	18	*U*=206, *Z*=0.334 *P*=0.668
Total HMR	220	102.5	197.5	135	*U*=186.5, *Z*=-0.129 *P*=0.899

8.4 Discussion

The major finding of this study was the identification of several relationships between cost-effective HMRs and factors that characterised them. Whilst not providing conclusive evidence, the findings generally support the hypothesis that certain factors may be used to predict cost-effective HMRs, which may ultimately be used to improve the cost-effectiveness of the HMR program.

8.4.1 Patient factors

Of the numerous patient factors investigated in the study, the only relationship identified involved a trend towards a greater proportion of highly cost-effective HMRs in older patients (*P*=0.078). This is consistent with the findings of several previous studies that older patients are more likely to experience DRPs and ADEs than younger patients.[11, 257, 258] However, the findings of the HOMER RCT by Holland *et al*. did not support the theory that HMRs are more likely to be cost-effective in older people.

This UK study investigated the effect of MMRs undertaken for patients aged >80 years who had recently been discharged from hospital. They found that their MMR model was not cost-effective compared to usual care, due to an increase in hospital readmissions in the MMR group.[25, 26] However, as outlined in Chapter One of this

thesis, the MMR model used in their study had significant differences to Australian HMRs, and it is potentially inappropriate to consider the interventions to be equivalent. Furthermore, in contrast to the HOMER study, only 5.6% of all the patients reviewed in the VALMER study had been recently discharged from hospital (as documented in the HMR referrals, Table 64). Based on these findings, it seems reasonable to suggest that one potential avenue to investigate improving the cost-effectiveness of HMRs is to specifically target very old patients, rather than those over 65 years.

The results of the analysis of patients taking drugs/ groups of specific interest are also notable. As discussed in the previous chapter, the VALMER study reported that HMRs were estimated to reduce the risk of myopathy (potentially due to HMG-CoA reductase inhibitors) and arrhythmias (possibly due to digoxin). However, based on the analysis presented in this chapter, there was no relationship between patients taking these particular drugs and either cost-effective or highly cost-effective HMRs. This may be interpreted as evidence that it is insufficient to simply direct HMRs at patients taking these drugs to improve the cost-effectiveness of HMRs. Such a strategy may improve some clinical outcomes related to use of these drugs, but not in a cost-effective way. The results of this study suggest that targeting other factors may be of more value in improving the cost-effectiveness of HMRs.

8.4.2 Pharmacist factors

The study found that the pharmacists who had performed the cost-effective and highly cost-effective HMRs reported undertaking a greater amount of continuing professional education than the pharmacists who did not perform cost-effective and highly cost-effective HMRs. There is no published literature that has investigated the influence of continuing education on the cost-effectiveness of HMRs. However, a number of studies have associated improved health outcomes with continuing education undertaken by other health professionals. A systematic review of the literature reported that continuing education for medical practitioners is associated with improvements in several clinical outcomes for patients, including arthritis pain, depression, general health and function.[299] Additionally, some studies have reported reduced numbers and duration of hospitalisation resulting from continuing education for medical practitioners.[299] Based on these findings, it is plausible that continuing

education may influence the cost-effectiveness of medical care provided by other health professionals, such as pharmacists.

The importance of continuing education has been recognised by the AACP for several years, as all accredited pharmacists are required to undertake a minimum level of continuing professional education each year to maintain their accreditation.[129] The results of this study suggest that additional pharmacist education may be worthy of investigation to improve the cost-effectiveness of HMRs. It is notable that several of the expert assessors commented that many of the recommendations made in the HMRs demonstrated an over-reliance on clinical guidelines without consideration of the patient's likely therapeutic objectives, as discussed previously. It is possible that continuing education in this area may be a promising target for improving the cost-effectiveness of HMRs.

8.4.3 Process factors

No previous literature has investigated the relationship between HMR referrals and the potential outcomes of HMRs. However, the results of the investigation into these relationships were somewhat counter-intuitive, but there are plausible explanations for most of the findings. Firstly, a greater proportion of HMRs with no indication for the HMR were highly cost-effective, compared to the HMRs with a reason for referral. There are two potential explanations for this. It is possible that in the HMRs where no reason for referral was documented, the pharmacists did not focus on the specific aspect/s of the patient as per the referral reason. Consequently, they may have identified DRPs of which the GP was not aware, and that were of high value once resolved. Alternatively, the association may be related to some GPs highlighting too many reasons for the HMR referral- more than one reason was documented in 36.5% of the HMRs (Table 64). In these HMRs, it is possible that the pharmacists did not know the aspects of the patient's therapy on which to focus, and so valuable DRPs were not resolved.

A greater proportion of HMRs with relevant pathology/ laboratory investigations were estimated to be highly cost-effective, compared to the HMRs without such information. This finding is consistent with anecdotal evidence from accredited pharmacists who greatly value this data being available when undertaking HMRs

(Appendix XXIV). In consideration of these findings, and that more than 95% of GPs now using computerised systems for patient management (which greatly simplify the generation of HMR referrals),[301] there seems to be little reason to not include recent and potentially relevant pathology/ laboratory data in HMR referrals.

The finding regarding the level of detail of medical history in the referrals is difficult to explain. Based on the findings of previous research, it was hypothesised that more detailed patient history in the HMR referral would improve the pharmacists' detection of DRPs and, consequently, may be related to improved clinical outcomes. [47, 291, 292] However, a greater proportion of HMRs with minimal medical history were estimated to be cost-effective, compared to the HMRs with detailed medical histories. In contrast, there was no relationship between the medical history detail and the highly cost-effective HMRs. Rather than conclude that pharmacists should be provided with minimal medical histories when undertaking HMRs, it is perhaps most appropriate to conclude from this finding that further investigation into the contents of HMR referrals may be warranted to optimise the HMR process.

8.4.4 Limitations

There are several limitations to this sub-study that must be considered when interpreting its results. Firstly, whether or not each HMR was initially categorised as cost-effective, highly cost-effective or otherwise, was largely based on expert forecasts. Although it was attempted to optimise the methodology used to develop the estimates of cost-effectiveness, the estimates could not be considered to be accurate measurements of costs and QOL. Furthermore, as discussed in the previous chapter, it was possible that the inclusion of other costs in the economic model used to generate estimates of cost-effectiveness was likely to have altered the costs resulting from each HMR. Hence, there is a reasonable likelihood that there were some inaccuracies in the cost-effectiveness classification of each HMR. In a larger sample, this limitation may have been of less importance; however, only 60 HMRs were used in this study and the limitation may have substantially confounded the results. Despite this, most of the results appear to be explainable in the context of existing literature, which suggests some degree of validity.

The small sample size resulted in limitations that affected the level of analysis that could be undertaken in the sub-study. Many of the factors that were investigated in the study were potentially inter-related. For example, it was identified that the medians of the number of HMRs ever completed and hours of continuing education undertaken in the previous year were higher in pharmacists who were capable of cost-effectiveness compared to those who were not. However, it could not be rigorously investigated whether these factors were interrelated. That is, if the pharmacists who had ever completed a greater number of HMRs had also undertaken more continuing education in the previous year. Similarly, there was no way to identify inter-relationships between the different types of factors, which needed to be investigated to draw more definitive conclusions from the results. For example, had the pharmacists who had undertaken more continuing education also submitted more HMRs performed for older patients, then this would have accounted for the findings regarding these factors. A substantially more elegant analysis using logistic regression may have been used to identify these inter-relationships and account for them.[300] Such an analysis would also have provided some indication as to the strength of the relationship between the various factors and the cost-effectiveness of the HMRs. However, in consideration of the number of factors that were investigated and consequently the sample size requirements of logistic regression,[300] it was not suitable to use this technique in this study. Indeed, for several of the drug/ groups of specific interest, the number of cases was at the limit of what is considered appropriate for simple χ^2 analyses,[302] and it is possible that some significant relationships were not identified due to insufficient data.

The small sample size also restricted the analysis of patient factors that could be undertaken. As discussed in the introduction to this chapter, there is some evidence that HMRs may be of benefit in patients with heart failure.[174, 285] The findings of the VALMER study reported in Chapter Six of this thesis suggested benefits were likely in patients with chronic airways disease. HMRs have also been promoted as being beneficial in patients with other chronic diseases (despite a lack of evidence), such as gout, urinary incontinence and osteoporosis.[303-305] However, the numbers of patients with these conditions were too small to analyse in this sub-study.

A final limitation relates to the grouping of the pharmacists according to whether or not they had performed cost-effective HMRs. The grouping system used was biased towards pharmacists who had more than one HMR in the analysis, as this increased their chances of a cost-effective HMR being included. Consequently, it is possible that the results of the factors relating to the pharmacists' characteristics are less robust than the patient and process factors.

8.5 Conclusions

The results of the study presented in this chapter provided some limited insight into the relationships between the HMRs in the VALMER study and factors that potentially influenced their cost-effectiveness. Although relationships between several types of factors and the cost-effectiveness of HMRs were identified, the analysis was undertaken retrospectively and it cannot be definitively concluded that these factors influenced the cost-effectiveness of the HMRs. Furthermore, there are several limitations to the analysis that may have adversely affected the validity of its findings. Nonetheless, the findings may be hypothesis-generating for further research to investigate whether these factors can be used to improve the cost-effectiveness of HMRs and the HMR program.

Chapter 9 - Conclusions

Despite widespread awareness of their prevalence in community-dwelling patients, DRPs continue to result in significant morbidity, mortality and financial costs in Australia and internationally.[7, 257, 258, 306-310] There is a clear need for clinically beneficial and cost-effective interventions that reduce the additional costs and QOL losses incurred by DRPs that result in medication misadventure. The knowledge of therapeutics and pharmacology possessed by pharmacists allows them to readily identify and make recommendations to resolve DRPs, with the ultimate intention of reducing healthcare costs and improving QOL.[27, 47, 54, 56, 61, 126, 146] The HMR program implemented in Australia over a decade ago is recognition of pharmacists' ability to achieve these potential benefits through the process of medication review.[116] The research presented in this thesis sought to investigate whether the HMR program was achieving these aims, and the program's cost-effectiveness.

As a result of the complexity involved in the assessment of HMRs, it was necessary to develop a novel methodology that generated estimates of costs, clinical outcomes and QOL effects of HMRs, primarily using expert opinion.[191] A significant outcome of this research was a table of common clinical consequences that may be avoided or result from the interventions made in HMRs. Linked to each consequence are estimates of the QOL effects and health resource utilisation incurred when a patient experiences the consequence. Although the consequences table was developed for the research presented in this thesis, its use in another study significantly contributed to a new paradigm for community pharmacy practice, whereby pharmacists are financially incentivised by the Australian government to undertake clinical interventions.[283]

There are several other findings from the research undertaken for this thesis that should direct further HMR research and potentially inform government policy regarding HMRs and the HMR program. Most importantly, the study's findings add further evidence to the issue that some HMRs are highly cost-effective, but too many HMRs are currently being performed that result in very little quantifiable improvement in QOL or cost savings.[26, 30, 86] Consequently, it must be a priority for further research to investigate ways to improve the targeting of HMRs towards patients most likely to benefit from them.

Limitations to the studies undertaken in this thesis prevented definitive identification of the factors that result in a greater likelihood of cost-effective HMRs. However, an association between a higher proportion of cost-effective HMRs in very old patients, and HMRs performed by pharmacists who undertook more continuing-education was identified. These findings may form the basis of further research into improving the cost-effectiveness of the HMR program via targeting the service to patients with specific characteristics, and developing educational materials to support accredited pharmacists to perform more patient-centred and clinically-beneficial HMRs.

In the absence of well-characterised factors that can be used to identify patients who will most likely benefit from HMRs, alternative strategies may be required to improve the cost-effectiveness of the HMR program. The planned implementation of Medicines Use Reviews (MURs) in Australia in 2012 may offer a timely opportunity to optimise the identification of potential HMR recipients.[311, 312] According to the four levels of medication review defined in *Room for Review*,[111] MURs are level 1 reviews whereby a pharmacist undertakes a medication review in-pharmacy without access to the patient's clinical notes or upon receipt of a GP's referral. The focus of MURs is to enhance adherence by improving patient knowledge and understanding of their medications,[313] without a clinical evaluation of the patient's therapy as is undertaken in HMRs. MUR programs have been implemented nation-wide in the UK and New Zealand, and have been trialled in Australia in recent years.[312, 314, 315]

As MURs require less time and arguably less training to perform,[113, 314] it is probable that the costs associated with providing them will be significantly lower than HMRs. In an Australian trial underway at the time of writing this thesis, pharmacists are reimbursed $60 for each MUR undertaken for non-diabetic patients, and $90 for diabetic patients.[311] This is comparable to the UK where pharmacies are reimbursed £28 per MUR,[313] and New Zealand, where payments range between NZD$101-$150 for three patient interviews to NZD$181-$200 for four interviews.[113]

Despite a paucity of literature that has investigated the clinical outcomes and cost-effectiveness of MURs,[315] it is likely that the outcomes in terms of patient acquisition of medicine information and reassurance will be similar to that provided in HMRs.[279] Hence, it is possible that MURs may facilitate the identification of patients who are likely to benefit from a full clinical medication review (that is, a HMR) and those for

whom an MUR alone is sufficient. In their review of the cost-effectiveness of medication reviews, Zermansky and Silcock stated that although full clinical medication review is seen as the gold standard, it may not always be necessary for every patient.[114] It therefore seems plausible that a two-tier medication review process involving both MUR and HMR may be more cost-effective than HMR alone and there is a strong argument to investigate such a model.

Another facet of the HMR process that is yet to be extensively researched is whether a home visit is integral to HMRs achieving beneficial outcomes. The current HMR model allows for locations other than the patient's home to be used for the patient interview. However, the very name of the HMR program implies that the resident's home is the preferred interview site. Moreover, despite many older patients reportedly appreciating the home visit,[15, 30] it has been identified as a barrier for younger patients to receive a HMR.[30] The median reported travel time in the VALMER study was 20 minutes, which accounted for approximately 10% of the total time to perform a HMR. It is possible that conducting the HMR interview at an alternative venue may contribute to optimising the HMR process. Of the five Australian QUM Evaluation Program projects, only the flawed study by Greenhill investigated undertaking HMRs in the GP surgery.[136] In contrast, several international studies of MMRs have involved the patient interview being performed at alternative sites, typically GP surgeries. [64, 146, 150, 173] Interviewing patients has been found to increase DRP detection rates,[316] but whether the additional costs incurred by undertaking the patient interview at their home are offset by the benefits should be investigated.

This issue is not isolated to HMRs - there is substantial debate in the literature regarding numerous interventions that involve home visits undertaken by medical practitioners and nurses throughout the world.[317-321] There are many government-funded programs implemented worldwide involving home visits. A systematic review of studies that investigated the effects of preventive home visits for elderly people living in the community by medical practitioners found no clear evidence in favour of the intervention.[319] A more recent systematic review of studies of intensive (at least four visits per 12 months) home-based interventions for elderly "at risk" patients concluded that the programs did not appear to be beneficial.[317] In contrast, a cost-utility analysis of a Swedish study of an intervention involving home visits by nurses was found to result in net savings, and was therefore cost-effective.[318] In consideration

of the need to optimise the HMR process as illustrated by this thesis, there is an argument for a comparative investigation of the effectiveness of HMRs undertaken at home versus a centralised location such as a GP surgery or community pharmacy. Should the interventions prove comparable in efficacy, the HMR reimbursement levels could then be reassessed.

Further recommendations from the research presented in this thesis result from limitations to the methodology used in the VALMER study. Despite the additional research undertaken to improve the robustness of the economic evaluation methodology developed by Tenni,[191] the results of the VALMER study remain largely based upon expert opinion and incorporate a number of major assumptions. As a consequence, there remains a need for a large-scale longitudinal RCT comparing the clinical outcomes and costs associated with HMRs to usual care, as described by Zermansky and Silcock.[114] Until such a study is conducted, the benefits and cost-effectiveness of the HMR program will remain uncertain.

A final concern raised by the findings of the research undertaken in this thesis involves another medication review program currently subsidised by the Australian government. The RMMR program was introduced for nursing home residents in 1997, with funding based primarily on the results of a single study undertaken by Roberts *et al*.[16] In that study, drug use in the RMMR group was reduced by 14.8% relative to the controls, which equated to an annual drug cost saving of $64 per resident. There was no change in several morbidity indices or survival. Since this study, the only published economic evaluation of the effectiveness of RMMRs is an evaluation of the first year of the RMMR program[xxi].[323] The evaluation again associated no significant improvement in morbidity indices or mortality resulting from RMMRs, although a cost-effective analysis estimated a potential net annual cost saving of $1151 per bed. However, as there was no significant difference between the RMMR and control patients in any of the variables used to generate this estimate, it may only be considered to be indicative. Furthermore, as with the HMR program, the remuneration paid to pharmacists and GPs for their

[xxi] An evaluation of the RMMR program that was conducted in 2010 included a cost-effectiveness analysis.[322] However, this was not a full economic evaluation and only investigated the implementation of the collaborative RMMR model and not the clinical or economic outcomes of RMMRs

involvement in RMMRs has increased considerably since 1997 (from $54 per bed per year to $201.95 in December 2011).[225]

There is scant international literature that has assessed the cost-effectiveness of pharmacist-conducted MMRs in nursing home residents, with most studies being simple cost- analyses.[324, 325] A comprehensive cost-effective analysis was recently undertaken alongside a trial of pharmaceutical care specifically targeting inappropriate prescribing of psychoactive drugs in nursing homes in Northern Ireland.[326] This study reported a high probability of the intervention being cost-effective, even at low thresholds of willingness to pay to avoid an inappropriately prescribed psychoactive drug. Nonetheless, this finding cannot be extrapolated to the Australian RMMR program as the MMR model used in the study was quite different to a RMMR. However, the VALMER study found that the HMR program may not be cost-effective as was predicted by initial research, so it is possible that the RMMR program may also be less cost-effective than is assumed. Given the lack of recent research into RMMRs, it is reasonable to suggest that there is also a need for investigation of the cost-effectiveness of the RMMR program.

In conclusion, the findings of this thesis add to the growing body of literature supporting the need for a targeted approach to HMRs to improve the cost-effectiveness of the HMR program. It is imperative for investigations into the determinants of cost-effective HMRs be made a priority. Once these factors are identified, strategies to more effectively target HMRs to patients who would benefit more from the service must be implemented to improve the cost-effectiveness and sustainability of the HMR program, otherwise it will likely become a target for disinvestment, despite the benefits for some patients being considerable.

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A CLINICAL AND ECONOMIC EVALUATION OF MEDICATION REVIEWS CONDUCTED BY PHARMACISTS FOR COMMUNITY-DWELLING AUSTRALIANS

Volume Three

Andrew Stafford BPharm(Hons) MPS AACPA

Appendix I - Ethics approval

COPY

Private Bag 01 Hobart
Tasmania 7001 Australia
Telephone (03) 6226 2764
Facsimile (03) 6226 7148
Marilyn.Knott@utas.edu.au
http://www.research.utas.edu.au//index.htm

MEMORANDUM

HUMAN RESEARCH ETHICS COMMITTEE (TASMANIA) NETWORK

UTAS

MINIMAL RISK APPLICATION APPROVAL

2 May 2007

Professor Gregory Peterson
Pharmacy
Private Bag 26
Hobart

Ethics reference: H9360

'Drug related problems identified in pharmacist-conducted medication reviews'

Student: Andrew Stafford (Honours)

Dear Professor Peterson

Acting on a mandate from the Tasmania Social Sciences HREC, the Chair of the committee considered and approved the above project on 2 May 2007.

All committees operating under the Human Research Ethics Committee (Tasmania) Network are registered and required to comply with the *National Statement on the Ethical Conduct in Research involving Humans 1999* (NHMRC guidelines).

Therefore, the Chief Investigator's responsibility is to ensure that:

1) All researchers listed on the application comply with HREC approved application.
2) Modifications to the application do not proceed until approval is obtained in writing from the HREC.
3) The confidentiality and anonymity of all research subjects is maintained at all times, except as required by law.
4) Clause 2.37 of the *National Statement* states:
   An HREC shall, as a condition of approval of each protocol, require that researchers immediately report anything which might warrant review of ethical approval of the protocol, including:
   a) *Serious or unexpected adverse effects on participants;*
   b) *Proposed changes in the application; and*
   c) *Unforeseen events that might affect continued ethical acceptability of the project.*

   The report must be lodged within 24 hours of the event to the Ethics Executive Officer who will report to the Chairs.

A PARTNERSHIP PROGRAM IN CONJUNCTION WITH THE DEPARTMENT OF HEALTH AND HUMAN SERVICES

5) All participants must be provided with the current Information Sheet and Consent form as approved by the Ethics Committee.

6) The Committee is notified if any investigators are added to, or cease involvement with, the project.

7) This study has approval for four years contingent upon annual review. An *Annual Report* is to be provided on the anniversary date of your approval. Your first report is due [12 months from 'Ethics Committee Approval' date]. You will be sent a courtesy reminder by email closer to this due date.
Clause 2.35 of the National Statement states:
As a minimum an HREC must require at regular periods, at least annually, reports from principal researchers on matters including:
   a) *Progress to date or outcome in case of completed research;*
   b) *Maintenance and security of records;*
   c) *Compliance with the approved protocol, and*
   d) *Compliance with any conditions of approval.*

8) A *Final Report* and a copy of the published material, either in full or abstract, must be provided at the end of project.

Yours sincerely

M. Knott

for **Ethics Executive Officer**

A PARTNERSHIP PROGRAM IN CONJUNCTION WITH THE DEPARTMENT OF HEALTH AND HUMAN SERVICES

Private Bag 01 Hobart
Tasmania 7001 Australia
Telephone (03) 6226 2764
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http://www.research.utas.edu.au//index.htm

MEMORANDUM

HUMAN RESEARCH ETHICS COMMITTEE (TASMANIA) NETWORK

UTAS

AMENDMENT TO EXISTING APPLICATION APPROVAL

4 December 2007

Professor Gregory Peterson
Pharmacy
Private Bag 26
Hobart

H9360: The economic value of home medicines reviews (The VALMER Project).
Other investigator: Peter Tenni
Honours student: Andrew Stafford

Dear Professor Peterson

The Tasmania Social Sciences Human Research Ethics Committee has approved the Amendment to the above project on 2nd of December 2007.

Amendment description:

The originally approved ethics project to be extended, as detailed on formal Ethics Amendment form. Extension of project will utilize the same methods employed in initial study, and the data will be managed in the same way. The only substantial change to original ethics submission is to conduct an economic analysis of the de-identified data collected, from a lager sample of pharmacists.

Yours sincerely

M. Knott

Ethics Executive Officer

for

A PARTNERSHIP PROGRAM IN CONJUNCTION WITH THE DEPARTMENT OF HEALTH AND HUMAN SERVICES

COPY

Private Bag 01 Hobart
Tasmania 7001 Australia
Telephone (03) 6226 2764
Facsimile (03) 6226 7148
Marilyn.Knott@utas.edu.au
http://www.research.utas.edu.au//index.htm

MEMORANDUM

HUMAN RESEARCH ETHICS COMMITTEE (TASMANIA) NETWORK

UTAS

AMENDMENT TO EXISTING APPLICATION APPROVAL

28 February 2008

Professor Gregory Peterson
Pharmacy
Private Bag 26
Hobart

Ethics reference: H9360

'The economic value of home medicines reviews (The VALMER Project)'

Student: Andrew Stafford (Honours)

Dear Professor Peterson

The Tasmania Social Sciences Human Research Ethics Committee has approved the Amendment to the above project on 26/2/2008.

Amendment description:

Permission sought to add an additional component to project - full details as per formal Ethics Amendment submitted for approval.

Yours sincerely

M. Knott

for **Ethics Executive Officer**

A PARTNERSHIP PROGRAM IN CONJUNCTION WITH THE DEPARTMENT OF HEALTH AND HUMAN SERVICES

Private Bag 01 Hobart
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MEMORANDUM

HUMAN RESEARCH ETHICS COMMITTEE (TASMANIA) NETWORK

UTAS

AMENDMENT TO EXISTING APPLICATION APPROVAL

30 June 2009

Professor Gregory Peterson
Pharmacy
Private Bag 26
Hobart

Ethics reference: H9360

The economic value of home medicines reviews (The VALMER Project).

Dear Professor Peterson

The Tasmania Social Sciences Human Research Ethics Committee has approved the Amendment to the above project on 24/6/2009.

Amendment description:

Ethics approval sought for sub-study to complement the pre-approved project methodology. Full details as per formal Ethics Amendment submitted for approval.

Yours sincerely

M. Knott

for **Ethics Executive Officer**

A PARTNERSHIP PROGRAM IN CONJUNCTION WITH THE DEPARTMENT OF HEALTH AND HUMAN SERVICES

Appendix II - Pharmacist consent form

Information Release Form

I, _____ (insert name)

☐ hereby give my permission (please tick)

for AACP to release my 2008 AACP survey and accreditation/reaccreditation MCQ results to the VALMER research team.

I understand that the AACP has given its permission for this information to be made available to the research team for the purposes of the VALMER study.

I understand that this information will be analysed in conjunction with HMR data I submit for inclusion in the VALMER study.

I understand that this information will be stored securely at all times, and that any publication/s resulting from this research will suitably de-identify this information.

I also understand that I may withdraw from the study at any point in time by notifying the research team.

My AACP MRN is _____ (insert MRN).

My email address is _____ (insert email address)

Signed Date _____

Please return this form to:

Andrew Stafford
School of Pharmacy
Private Bag 83
University of Tasmania
Hobart 7001

This project has been granted ethics approval by the Human Research Ethics Committee (Tasmania) Network (H9368), and is funded by the Australian Government Department of Health and Ageing as part of the Fourth Community Pharmacy Agreement through the Fourth Community Pharmacy Agreement Grants Program managed by the Pharmacy Guild of Australia

Appendix III - VALMER study Outcomes Summary Form

VALMER Study

Home Medicine Review Submission

Reviewing pharmacist MRN: _____ **Date of Review:** _____

Patient Date of Birth: _____ **Patient gender:** M / F
(please circle)

Time taken to perform this HMR

Preparation before the interview: _____ **minutes**

Patient interview: _____ **minutes**

Travel: _____ **minutes**

Assessment report: _____ **minutes**

Other time (please specify): _____

_____

_____

Please send this form, the following page, and de-identified copies of the referral and clinical assessment report to:

Andrew Stafford
Private Bag 26
University of Tasmania
Hobart 7001

Don't forget to also send an invoice for up to five reviews!

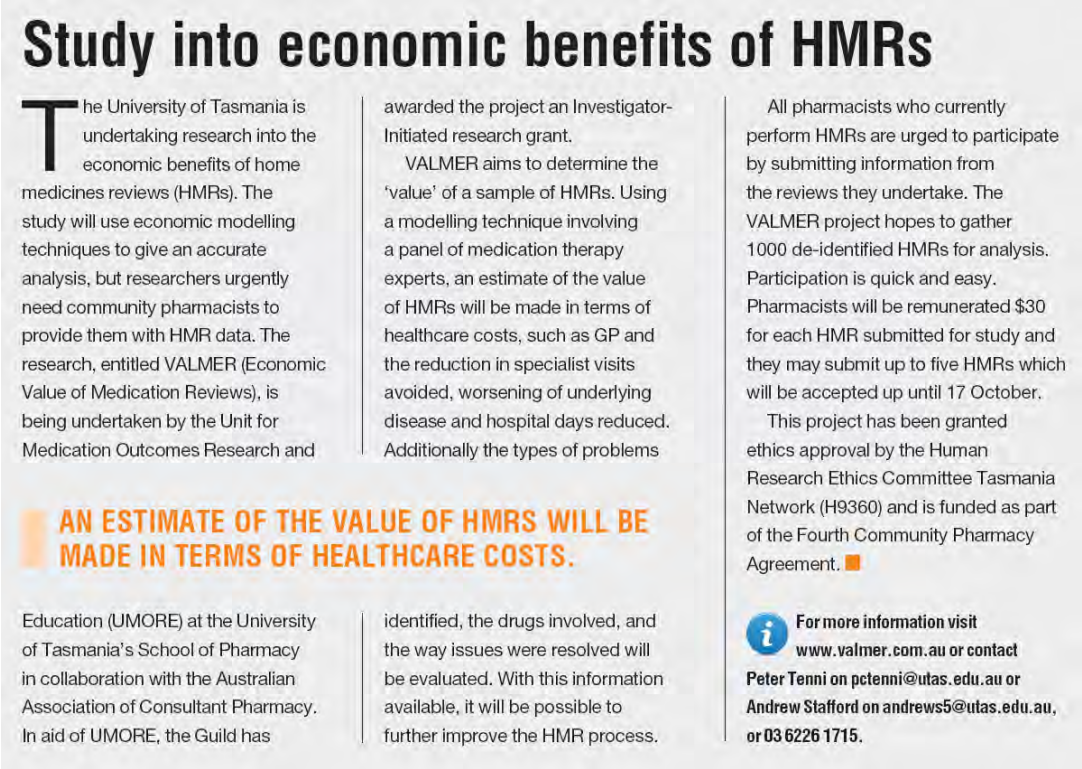
This project has been granted ethics approval by the Human Research Ethics Committee (Tasmania) Network (H9360), and is funded by the Australian Government Department of Health and Ageing as part of the Fourth Community Pharmacy Agreement through the Fourth Community Pharmacy Agreement Grants Program managed by the Pharmacy Guild of Australia

Outcomes Summary

Findings and Recommendations	GP's action regarding this recommendation
Example *Reduce allopurinol dose from 300mg to 100mg daily as patient has a creatinine clearance of 20mL/min*	*GP reduced dose to 150mg daily*
One	
Two	
Three	

This project has been granted ethics approval by the Human Research Ethics Committee (Tasmania) Network (H9360), and is funded by the Australian Government Department of Health and Ageing as part of the Fourth Community Pharmacy Agreement through the Fourth Community Pharmacy Agreement Grants Program managed by the Pharmacy Guild of Australia

Appendix IV - Project promotion (print media)



Study into economic benefits of HMRs

The University of Tasmania is undertaking research into the economic benefits of home medicines reviews (HMRs). The study will use economic modelling techniques to give an accurate analysis, but researchers urgently need community pharmacists to provide them with HMR data. The research, entitled VALMER (Economic Value of Medication Reviews), is being undertaken by the Unit for Medication Outcomes Research and Education (UMORE) at the University of Tasmania's School of Pharmacy in collaboration with the Australian Association of Consultant Pharmacy. In aid of UMORE, the Guild has awarded the project an Investigator-Initiated research grant.

VALMER aims to determine the 'value' of a sample of HMRs. Using a modelling technique involving a panel of medication therapy experts, an estimate of the value of HMRs will be made in terms of healthcare costs, such as GP and the reduction in specialist visits avoided, worsening of underlying disease and hospital days reduced. Additionally the types of problems identified, the drugs involved, and the way issues were resolved will be evaluated. With this information available, it will be possible to further improve the HMR process.

AN ESTIMATE OF THE VALUE OF HMRS WILL BE MADE IN TERMS OF HEALTHCARE COSTS.

All pharmacists who currently perform HMRs are urged to participate by submitting information from the reviews they undertake. The VALMER project hopes to gather 1000 de-identified HMRs for analysis. Participation is quick and easy. Pharmacists will be remunerated $30 for each HMR submitted for study and they may submit up to five HMRs which will be accepted up until 17 October.

This project has been granted ethics approval by the Human Research Ethics Committee Tasmania Network (H9360) and is funded as part of the Fourth Community Pharmacy Agreement.

For more information visit www.valmer.com.au or contact Peter Tenni on pctenni@utas.edu.au or Andrew Stafford on andrews5@utas.edu.au, or 03 6226 1715.

FIGURE 58 - EXAMPLE OF PROJECT PROMOTION (AUSTRALIAN JOURNAL OF PHARMACY 2009;89:22)

Appendix V - Pharmacy Guild of Australia media release

The Pharmacy Guild of Australia

16 April 2008

Media release

UTas study into economic benefits of HMRs

The University of Tasmania is currently undertaking research into the economic benefits of Home Medicines Reviews (HMRs). The study will use sophisticated economic modelling techniques to give an accurate analysis, but researchers urgently need community pharmacists to provide them with HMR data.

The research, entitled VALMER (Economic Value of Medication Reviews), is being undertaken by the Unit for Medication Outcomes Research and Education (UMORE) at the University of Tasmania's School of Pharmacy in collaboration with the Australian Association of Consultant Pharmacy. In aid of UMORE, the Pharmacy Guild of Australia has awarded the project an Investigator-Initiated research grant.

VALMER aims to determine the "value" of a sample of HMRs. Using a modelling technique involving a panel of medication therapy experts, an estimate of the value of HMRs will be made in terms of healthcare costs, such as GP and specialist visits avoided, worsening of underlying disease and hospital days avoided. Additionally the types of problems identified, the drugs involved, and the ways problems are resolved will be evaluated. With this information available, it will be possible to further improve the HMR process.

All pharmacists who currently perform HMRs are urged to participate by submitting information from the reviews they undertake. The VALMER project is aiming to gather 1000 de-identified HMRs for analysis. Participation is quick and easy. Pharmacists will be remunerated $30 for each HMR submitted for study and pharmacists may submit up to five HMRs which will be accepted up until 17 October this year.

This project has been granted ethics approval by the Human Research Ethics Committee (Tasmania) Network (H9360) and is funded by the Australian Government Department of Health and Ageing as part of the Fourth Community Pharmacy Agreement, through the Fourth Community Pharmacy Agreement Grants Program managed by the Pharmacy Guild of Australia.

For more information, please visit www.valmer.com.au or contact Peter Tenni - pctenni@utas.edu.au or Andrew Stafford -andrews5@utas.edu.au, 03 6226 1715.

National Secretariat
Level 2, 15 National Circuit, Barton, ACT 2600 Australia · PO Box 7036, Canberra Business Centre, ACT 2610 Australia
Telephone: + 61 2 6270 1888 · Facsimile: + 61 2 6270 1800 · E-mail: guild.nat@guild.org.au · Internet: www.guild.org.au

Appendix VI - VALMER project newsletters

Unit for Medications Outcomes Research and Education
University of Tasmania

www.valmer.com.au
VALMER AACP UTAS
The Value of Home Medicines Reviews

Project Update

Volume 1, Issue 1
June 2008

Pharmacist participation urgently required!

June 2008: Despite widespread promotion, pharmacist participation in the VALMER project has so far been disappointing.

After a recruiting drive at the AACP ConPharm seminar late last month, the number of pharmacists presently enrolled in the study is 75. Furthermore, only five pharmacists have submitted HMR data, for a total of 21 reviews.

The target numbers for participation are for 1000 HMRs to be submitted by over 200 pharmacists. Without an adequate amount of data, the study sample cannot be considered to be representative of the greater body of accredited pharmacists- so the project will only be successful with a high level of pharmacist participation. The results of the VALMER study may have significant ramifications on funding for the HMR program, hence all pharmacists performing HMRs should consider contributing by submitting reviews.

Data collection ends in October this year, so there is still plenty of time for pharmacists to participate. Participation is easy, well-reimbursed and not time-consuming. Pharmacists interested in the VALMER study should visit www.valmer.com.au for more information.

So I'm enrolled in VALMER – what do I do now?

Once a pharmacist has enrolled in the VALMER study, the next thing for them to do is start collecting information from the *next* HMRs that they perform. It is really important that pharmacists do not select the reviews that they submit in any way.

For each review, pharmacists are requested to provide de-identified copies of both the referral and their letter back to the doctor that contains their recommendations.

In addition to these two pieces of information, pharmacists should complete an Outcomes Summary form (available to download from the project website) for each HMR. This form details the outcomes of the first three recommendations made by the pharmacist in the HMR report. This form is completed by the pharmacist by contacting the doctor some weeks after the HMR to find out the outcomes of the review.

Once this information has been collected (for up to five HMRs), all that is left to do is post the data to VALMER, Private Bag 83, UTAS, Hobart 7001. Pharmacists may also include an invoice for $30 per HMR.

VALMER goes to ConPharm

May 2008: Pharmacists attending the AACP ConPharm seminar in Adelaide last month were given the chance to win a bottle of Jansz wine simply by enrolling in the VALMER study.

Over fifty pharmacists enrolled in the study during the three days of the conference. The winner of the competition for the bottle of Jansz cuvée was Elisabeth Sabolch of New South Wales. Congratulations Elisabeth, and thank you to all the pharmacists who enrolled in the study at ConPharm.

The VALMER project has been granted ethics approval by the Human Research Ethics Committee (Tasmania) Network (H9360). It is funded by the Australian Government Department of Health and Ageing as part of the Fourth Community Pharmacy Agreement through the Fourth Community Pharmacy Agreement Grants Program managed by the Pharmacy Guild of Australia

Project statistics (June 2008):

- Pharmacists enrolled: 75
- Target enrolment: 200 pharmacists
- HMRs submitted: 21
- Target HMRs: 1000
- Data collection ends: 17 October 2008

Contact:

Project Pharmacist:

Andrew Stafford

andrew.stafford@utas.edu.au

03 6226 1715

Private Bag 83
UTAS Hobart 7001

UMORE

FIGURE 59 - VALMER PROJECT NEWSLETTER JUNE 2008

Unit for Medications Outcomes Research and Education
University of Tasmania

www.valmer.com.au
VALMER AACP UTAS
The Value of Home Medicines Reviews

Project Update

Volume 1, Issue 2
June 2008

New participation requirements – outcomes information easier to obtain, no longer essential

24 June 2008: Due to difficulties in pharmacists obtaining information about HMR outcomes, the VALMER project methodology has been changed. Now there is no excuse for not getting involved in VALMER!

Many pharmacists have cited an inability to obtain information about HMR outcomes as a barrier to participating in the VALMER study. Despite their best efforts, obtaining this information from GPs has proven extremely difficult. Two changes have therefore been made to the project methodology to help these pharmacists participate in the VALMER project.

The first of these changes is a modified "Outcomes Summary" form. This form details the outcomes of the first three recommendations made by the pharmacist in the HMR report. The new version of this form may be directly attached to the HMR report that is sent to the GP. The GP then simply fills in the necessary outcome information and faxes it back to the reviewing pharmacist. This form (along with a de-identified copy of the referral and HMR report) may then be submitted for inclusion in the VALMER study.

For every HMR that is submitted with outcomes information, the reviewing pharmacist is now eligible to claim $60.

If there is no response from the GP (either from using this new form or by telephoning them directly), then an HMR may be submitted with only a de-identified copy of the referral and HMR report. Whilst it is highly desirable to have outcomes information provided with HMR data, an inability to collect outcomes information is no longer a reason to not participate in VALMER.

For each HMR that is submitted with just a referral and HMR report, pharmacists are reimbursed $20.

A flow chart for HMR submission may be found on page 2 of this newsletter.

Data collection ends mid-October this year, so there is still plenty of time for pharmacists to participate. As previously, it is really important that pharmacists do not select the reviews that they submit in any way. Each pharmacist may submit a maximum of 5 HMRs in total. All data may be sent to VALMER, Private Bag 83, UTAS, Hobart 7001.

Pharmacists interested participating in the VALMER study should visit www.valmer.com.au for more information. Alternatively, contact either Peter Tenni (pctenni@utas.edu.au) or Andrew Stafford (andrews5@utas.edu.au or 03 6226 1715) at the University of Tasmania.

The target numbers for participation are for 1000 HMRs to be submitted by over 200 pharmacists. Without an adequate amount of data, the study sample cannot be considered to be representative of the greater body of accredited pharmacists. This project will only be successful with a high level of pharmacist participation. The results of the VALMER study may have significant ramifications on funding for the HMR program; hence all pharmacists performing HMRs should consider contributing by submitting reviews.

The VALMER project has been granted ethics approval by the Human Research Ethics Committee (Tasmania) Network (H9360). It is funded by the Australian Government Department of Health and Ageing as part of the Fourth Community Pharmacy Agreement through the Fourth Community Pharmacy Agreement Grants Program managed by the Pharmacy Guild of Australia

Project statistics (End June 2008):

- Pharmacists enrolled: 84
- Target enrolment: 200 pharmacists
- HMRs submitted: 32
- Target HMRs: 1000
- Data collection ends: 17 October 2008

Contact:

Project Pharmacist:

Andrew Stafford
andrew.stafford@utas.edu.au
03 6226 1715
Private Bag 26
UTAS Hobart 7001

UMORE

FIGURE 60 - VALMER PROJECT NEWSLETTER JULY 2008

Unit for Medications Outcomes Research and Education
University of Tasmania

www.valmer.com.au
VALMER AACP UTAS
The Value of Home Medicines Reviews

Project Update

Last chance to get involved in VALMER!

30 September 2008: With just over a fortnight for data collection remaining, any pharmacist wanting to get involved in the VALMER study should do so as soon as possible.

Many of the pharmacists who have enrolled in the study have not yet submitted any HMRs. These pharmacists in particular should finalise their HMR submissions to ensure that they make the October 17 data collection cut-off.

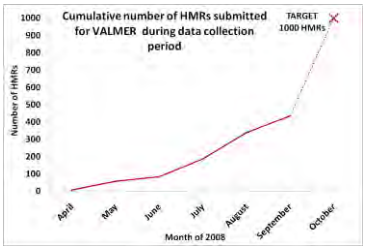
For each review, pharmacists are requested to provide de-identified copies of both the referral and their letter back to the doctor that contains their recommendations. In addition to these two pieces of information, pharmacists should ideally complete an Outcomes Summary form which details the outcomes of the first three recommendations made by the pharmacist in the HMR report. If it's not possible to obtain outcome information, however, a HMR may still be submitted for inclusion in the study.

Participating pharmacists should remember that it is really important that they do not select the reviews that they submit in any way.

Each pharmacist may submit a maximum of 5 HMRs in total, and will be reimbursed between $20 and $60 per HMR, depending upon the amount of information they provide for each HMR.

Pharmacists wanting more information about the VALMER study should visit the project website (www.valmer.com.au) or contact either Peter Tenni or Andrew Stafford at the University of Tasmania on 03 6226 1715.

As shown below, the target is to collect 1000 HMRs. With a big effort in these last two weeks, we might get close!



What happens when data collection ends?

30 September 2008: With the data collection period for the VALMER study closing shortly, preparations for the next stage of the project are being finalised.

During the past two months, a web-based HMR assessment system has been developed. This system will be used by a panel of "medication therapy experts" consisting of pharmacists, general practitioners and specialist medical practitioners. Over a three month period, these experts will use the online system to predict the likely outcomes of the interventions made by pharmacists in the HMRs submitted for the VALMER study.

Once the online assessment process has been completed, an estimate of the projected impact of each HMR on patient health is obtained. Appropriate economic analysis of the data will then be undertaken to provide an estimate of the average value of an HMR, which can then be used to estimate the benefits of HMRs Australia-wide.

The project will be completed in Sept 2009.

The VALMER project has been granted ethics approval by the Human Research Ethics Committee (Tasmania) Network (H9360). It is funded by the Australian Government Department of Health and Ageing as part of the Fourth Community Pharmacy Agreement through the Fourth Community Pharmacy Agreement Grants Program managed by the Pharmacy Guild of Australia

Volume 2, Issue 2
September 2008

Project statistics (End September 2008):

- Pharmacists enrolled: 156
- Target enrolment: 200 pharmacists
- HMRs submitted: 413
- Target HMRs: 1000
- Data collection ends: 17 October 2008

Contact:

Project Pharmacist:

Andrew Stafford
andrew.stafford@utas.edu.au
03 6226 1715
Private Bag 26
UTAS Hobart 7001

UMORE

FIGURE 61 - VALMER PROJECT NEWSLETTER SEPTEMBER 2008

Unit for Medications Outcomes Research and Education
University of Tasmania

www.valmer.com.au
VALMER AACP UTAS
The Value of Home Medicines Reviews

Project Update

HMR submission deadline extended!

Volume 3, Issue 1
October 2008

1 October 2008: Pharmacists now have an extra month to collect HMR data for the VALMER study.

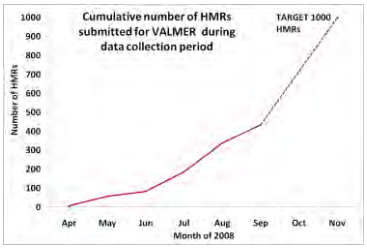
The original cut-off date for HMR submissions was 17 October this year. Owing to a slow start to data collection (see figure), this date has now been extended to **14 November** this year.

Many of the pharmacists who have enrolled in the study have not yet submitted any HMRs. The extra month for data collection will allow these pharmacists in particular to finalise their HMR submissions and contribute to the study. Pharmacists who have not yet enrolled in the study are also welcome to get involved and submit some HMRs.

For each HMR they submit, pharmacists are requested to provide de-identified copies of both the referral and their letter back to the doctor that contains their recommendations. In addition to these two pieces of information, pharmacists should ideally complete an Outcomes Summary form which details the outcomes of the first three recommendations made by the pharmacist in the HMR report. If it's not possible to obtain outcome information, a HMR may still be submitted for inclusion in the study.

Participating pharmacists should remember that it is really important that they do not select the reviews that they submit in any way. Each pharmacist may submit a maximum of 5 HMRs in total, and will be reimbursed between $20 and $60 per HMR, depending upon the amount of information they provide for each HMR.

Pharmacists wanting more information about the VALMER study should visit the project website (www.valmer.com.au) or contact either Peter Tenni or Andrew Stafford at the University of Tasmania on 03 6226 1715.



Project statistics (End September 2008):

- Pharmacists enrolled: 156
- Target enrolment: 200 pharmacists
- HMRs submitted: 413
- Target HMRs: 1000
- Data collection ends: 14 November 2008

What happens when data collection ends?

30 September 2008: With the data collection period for the VALMER study closing shortly, preparations for the next stage of the project are being finalised.

During the past two months, a web-based HMR assessment system has been developed. This system will be used by a panel of "medication therapy experts" consisting of pharmacists, general practitioners and specialist medical practitioners. Over a three month period, these experts will use the online system to predict the likely outcomes of the interventions made by pharmacists in the HMRs submitted for the VALMER study.

Once the online assessment process has been completed, an estimate of the projected impact of each HMR on patient health is obtained. Appropriate economic analysis of the data will then be undertaken to provide an estimate of the average value of an HMR, which can then be used to estimate the benefits of HMRs Australia-wide.

The project will be completed in Sept 2009.

The VALMER project has been granted ethics approval by the Human Research Ethics Committee (Tasmania) Network (H9360). It is funded by the Australian Government Department of Health and Ageing as part of the Fourth Community Pharmacy Agreement through the Fourth Community Pharmacy Agreement Grants Program managed by the Pharmacy Guild of Australia

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UMORE
Unit for Medications Outcomes Research and Education

FIGURE 62 - VALMER PROJECT NEWSLETTER OCTOBER 2008

Unit for Medications Outcomes Research and Education
School of Pharmacy, University of Tasmania

www.valmer.com.au
VALMER AACP UTAS
The Value of Home Medicines Reviews

Project Update

Volume 3, Issue 1
March 2009

VALMER survey now online!

25 March 2009: A short survey is now online for pharmacists who submitted HMRs for the VALMER study. The survey asks some general questions about the medication reviews that the pharmacists completed in 2008. Completing the survey will give participants the opportunity to win two bottles of premium Tasmanian wine.

Similar to last year's AACP accredited pharmacist survey, the VALMER survey also examines several areas of medication review practice. These include major area of employment, numbers of HMRs completed and RMMR experience. The survey also explores some key areas of collaboration between pharmacists and GPs, such as HMR referrals and medication management plans.

All pharmacists who submitted HMRs for the VALMER study are asked to complete the survey. The survey should take no more than 10 minutes to complete. Every pharmacist who completes the survey before June 19 this year will be given the opportunity to win two bottles of Jansz sparkling wine.

The survey can be accessed online at the study website www.valmer.com.au.

What's the word from VALMER so far?

Following the conclusion of HMR submissions for the VALMER study, a substantial amount of analysis has been undertaken to assess their "value". The analysis of the reviews will continue for another few months before the study concludes in September this year.

One hundred and forty-nine pharmacists submitted 661 HMRs for inclusion in the study. Each Australian state or territory was represented by at least one pharmacist, with the majority of pharmacists (57%) from either New South Wales or Victoria.

The general characteristics of the patients who were reviewed in the HMRs are shown in the table below. As expected, most were elderly patients with several co-morbidities taking multiple medications. The most common diagnosed medical conditions included hypertension (61% of patients), dyslipidaemia (41%) and Type II diabetes (33%). Correspondingly, over 70% of the sample were taking an antithrombotic agent (primarily aspirin) and a lipid modifying agent.

Pharmacists identified over 2300 drug-related problems in the sample. The most common problem identified was inadequate treatment of a condition, such as arthritic pain and hypertension. Other frequently occurring problems were lack of treatment for a condition, and identification of potential or actual adverse effects.

Around 2700 recommendations were made to resolve these problems. The most frequently made recommendations included performing laboratory monitoring, commencing a new medication, or ceasing another.

More preliminary results from VALMER will be presented at AACP's ConPharm conference on the Gold Coast in May this year.

	Mean age ± SD [range] (years)	Medical conditions Mean ± SD [range]	Medications Mean ± SD [range]
Females n= 383 (58%)	77 ± 10.3 [31 - 98]	9.1 ± 5.2 [0 - 29]	12.2 ± 4.5 [4 - 30]
Males n= 278 (42%)	75 ± 10.6 [30 - 96]	8.4 ± 4.9 [0 - 33]	11.1 ± 4.4 [2 - 28]

The VALMER project has been granted ethics approval by the Human Research Ethics Committee (Tasmania) Network (H9360). It is funded by the Australian Government Department of Health and Ageing as part of the Fourth Community Pharmacy Agreement through the Fourth Community Pharmacy Agreement Grants Program managed by the Pharmacy Guild of Australia

Project statistics (March 2009):

- Participating pharmacists: 149
- HMRs submitted: 661
- Project ends: September 2009

Contact:

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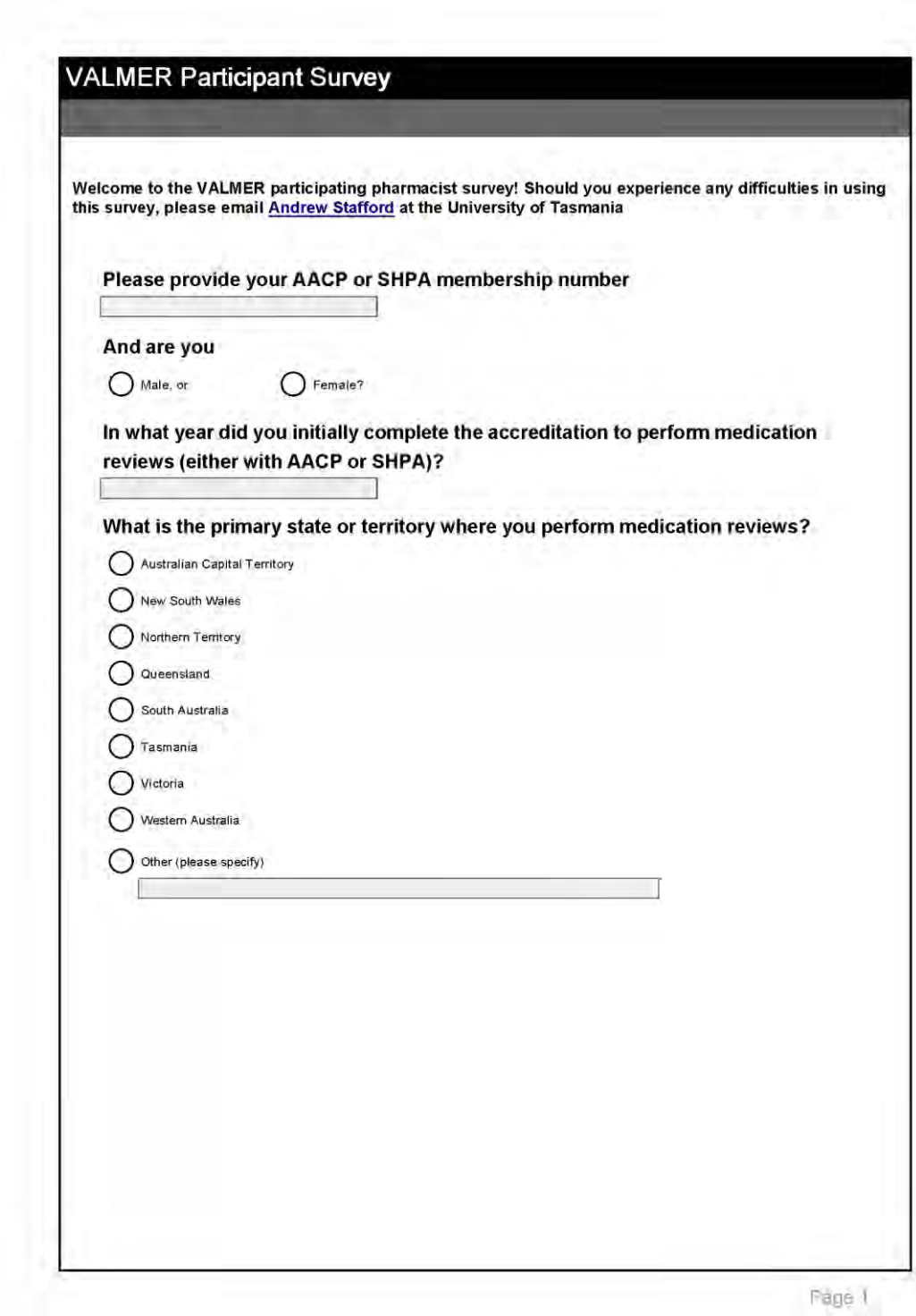
UMORE

FIGURE 63 - VALMER PROJECT NEWSLETTER MARCH 2009

Appendix VII - VALMER study pharmacist survey



VALMER Participant Survey

Welcome to the VALMER participating pharmacist survey! Should you experience any difficulties in using this survey, please email Andrew Stafford at the University of Tasmania

Please provide your AACP or SHPA membership number

And are you

○ Male, or ○ Female?

In what year did you initially complete the accreditation to perform medication reviews (either with AACP or SHPA)?

What is the primary state or territory where you perform medication reviews?

- ○ Australian Capital Territory
- ○ New South Wales
- ○ Northern Territory
- ○ Queensland
- ○ South Australia
- ○ Tasmania
- ○ Victoria
- ○ Western Australia
- ○ Other (please specify)

Page 1

VALMER Participant Survey

Your education history

In what year did you complete your initial undergraduate pharmacy course?

In which state did you complete this qualification?

- ◯ New South Wales
- ◯ Victoria
- ◯ South Australia
- ◯ Western Australia
- ◯ Tasmania
- ◯ Northern Territory
- ◯ Australian Capital Territory
- ◯ Queensland
- ◯ Overseas (please specify)

If applicable, please indicate any clinical pharmacy-related post-graduate qualifications you have completed:

- ☐ Post Graduate Diploma
- ☐ Masters
- ☐ Doctor of Philosophy

Other (please specify)

Please estimate how many hours of pharmacy-related continuing education you complete each year:

Please indicate whether or not you attended the following Continuing Education events in 2008:

	Attended	Did not attend
AACP Accredited pharmacist forum, Australian Professional Pharmacy Conference, Gold Coast	◯	◯
ConPharm Conference, Adelaide	◯	◯
AACP Accredited pharmacist forum, Pharmacy Australia Congress, Perth	◯	◯

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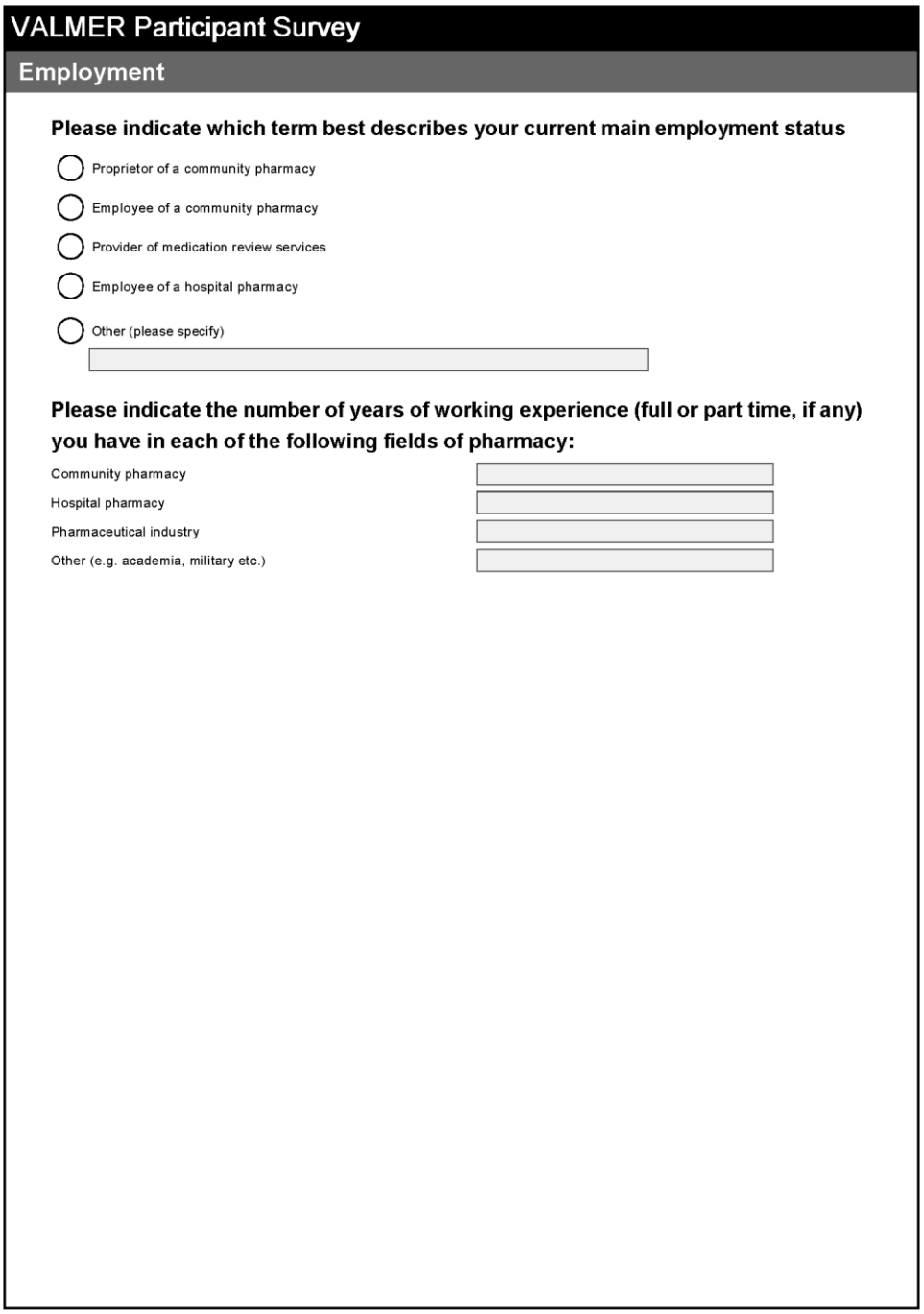

VALMER Participant Survey

Employment

Please indicate which term best describes your current main employment status

- ◯ Proprietor of a community pharmacy
- ◯ Employee of a community pharmacy
- ◯ Provider of medication review services
- ◯ Employee of a hospital pharmacy
- ◯ Other (please specify)

Please indicate the number of years of working experience (full or part time, if any) you have in each of the following fields of pharmacy:

Community pharmacy	
Hospital pharmacy	
Pharmaceutical industry	
Other (e.g. academia, military etc.)	

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VALMER Participant Survey

Focus of medication review

Please indicate the emphasis you usually place on each of the following processes when performing a HMR:

	None	Minimal	Some	Moderate	Most
Checking compliance:	○	○	○	○	○
Providing patient education (eg counseling, confusion re generics, pricing etc):	○	○	○	○	○
Assessing clinical appropriateness of drug therapy (eg doses rational, therapy consistent with current guidelines, identifying untreated indications):	○	○	○	○	○
Removing out of date and unnecessary prescriptions and repeat forms:	○	○	○	○	○
Identifying adverse drug reactions:	○	○	○	○	○
Checking administration equipment and technique (eg nebulisers, inhalers):	○	○	○	○	○
Ensuring adequate therapeutic monitoring:	○	○	○	○	○

Please indicate your level of agreement with the following statements about HMRs:

	Never	Sometimes	About half the time	Usually	Always
I am satisfied with the amount of information provided in HMR referrals	○	○	○	○	○
The patient interview significantly impacts on my findings in HMRs	○	○	○	○	○
I report every problem (actual or potential) I identify in a HMR	○	○	○	○	○
I prioritise the problems I identify in a HMR from most important to least important	○	○	○	○	○
I make recommendations to resolve the problems I identify in HMRs	○	○	○	○	○

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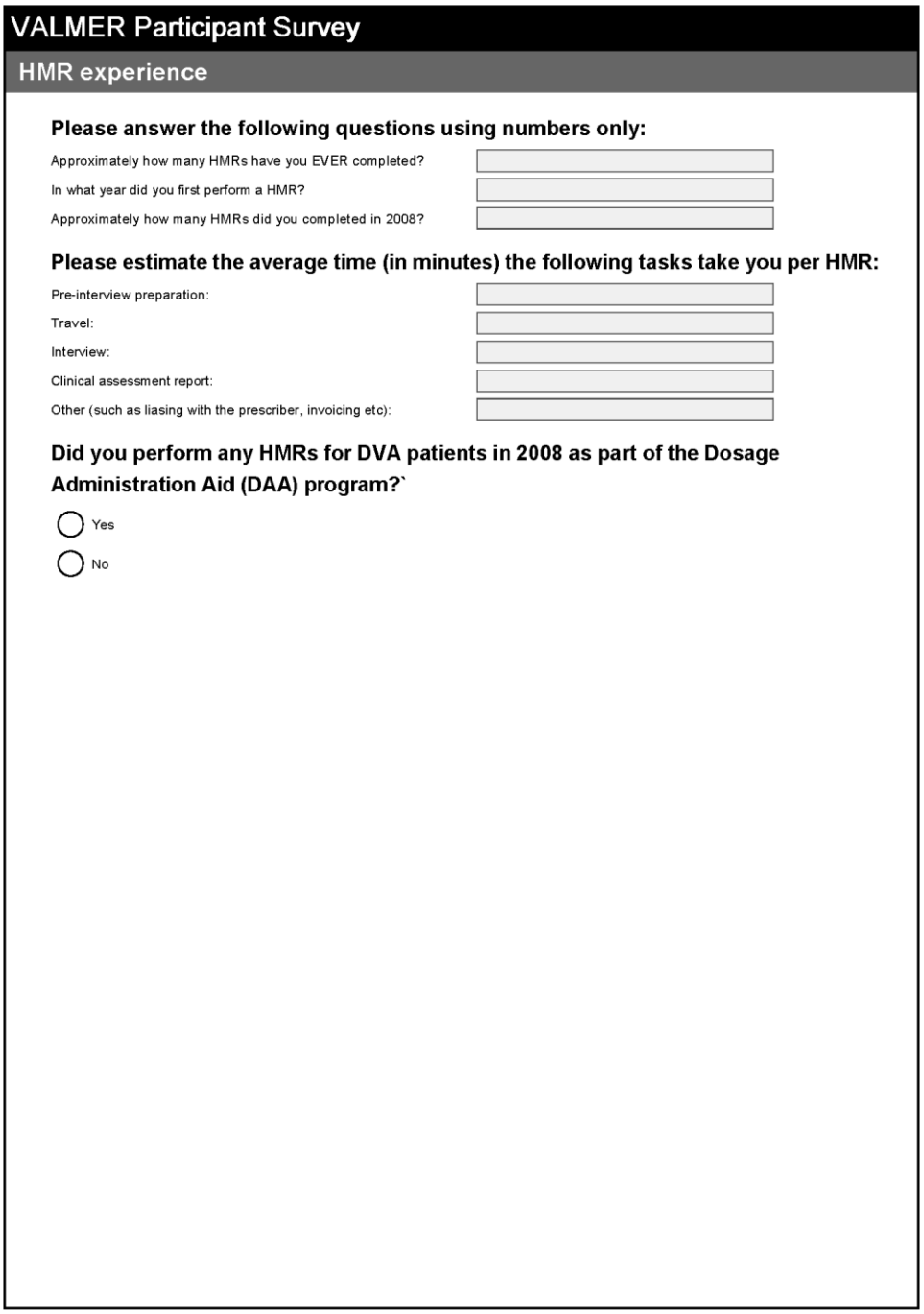

VALMER Participant Survey

HMR experience

Please answer the following questions using numbers only:

Approximately how many HMRs have you EVER completed?

In what year did you first perform a HMR?

Approximately how many HMRs did you completed in 2008?

Please estimate the average time (in minutes) the following tasks take you per HMR:

Pre-interview preparation:

Travel:

Interview:

Clinical assessment report:

Other (such as liasing with the prescriber, invoicing etc):

Did you perform any HMRs for DVA patients in 2008 as part of the Dosage Administration Aid (DAA) program?`

◯ Yes

◯ No

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VALMER Participant Survey

HMRs for the DVA DAA program

Thinking about the HMRs that you performed for DVA patients as part of the DAA program, please indicate if you feel that they were different to "normal" HMRs in the following aspects:

	Substantially more than a "normal" HMR	Somewhat more than a "normal" HMR	About the same as a "normal" HMR	Somewhat less than a "normal" HMR	Substantially less than a "normal" HMR
Complexity	◯	◯	◯	◯	◯
Number of compliance issues	◯	◯	◯	◯	◯
Number of clinical issues (adverse reactions, interactions, need for monitoring etc)	◯	◯	◯	◯	◯
Potential to improve the patient's outcomes	◯	◯	◯	◯	◯

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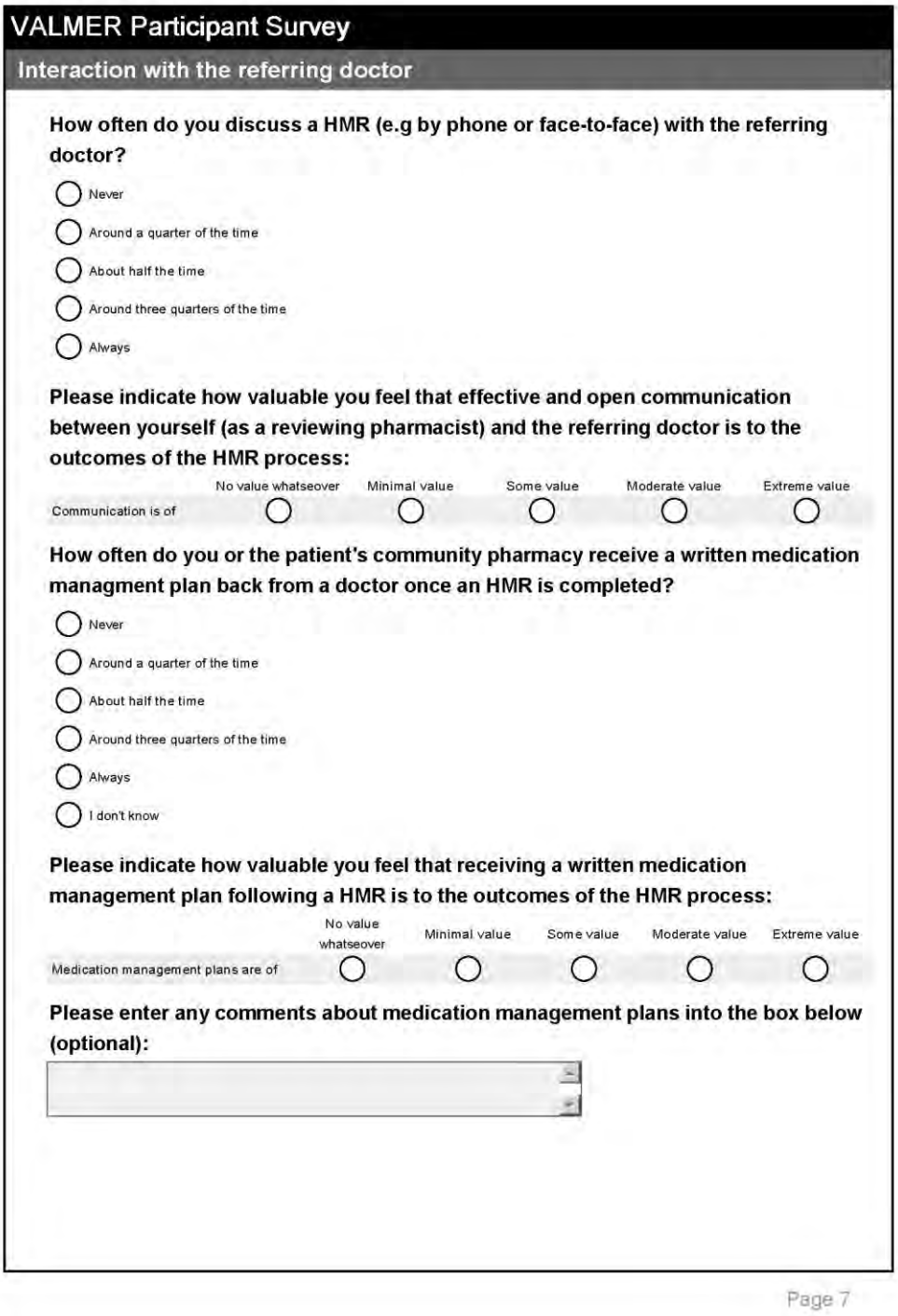

VALMER Participant Survey

Interaction with the referring doctor

How often do you discuss a HMR (e.g by phone or face-to-face) with the referring doctor?

- ◯ Never
- ◯ Around a quarter of the time
- ◯ About half the time
- ◯ Around three quarters of the time
- ◯ Always

Please indicate how valuable you feel that effective and open communication between yourself (as a reviewing pharmacist) and the referring doctor is to the outcomes of the HMR process:

	No value whatseover	Minimal value	Some value	Moderate value	Extreme value
Communication is of	◯	◯	◯	◯	◯

How often do you or the patient's community pharmacy receive a written medication managment plan back from a doctor once an HMR is completed?

- ◯ Never
- ◯ Around a quarter of the time
- ◯ About half the time
- ◯ Around three quarters of the time
- ◯ Always
- ◯ I don't know

Please indicate how valuable you feel that receiving a written medication management plan following a HMR is to the outcomes of the HMR process:

	No value whatseover	Minimal value	Some value	Moderate value	Extreme value
Medication management plans are of	◯	◯	◯	◯	◯

Please enter any comments about medication management plans into the box below (optional):

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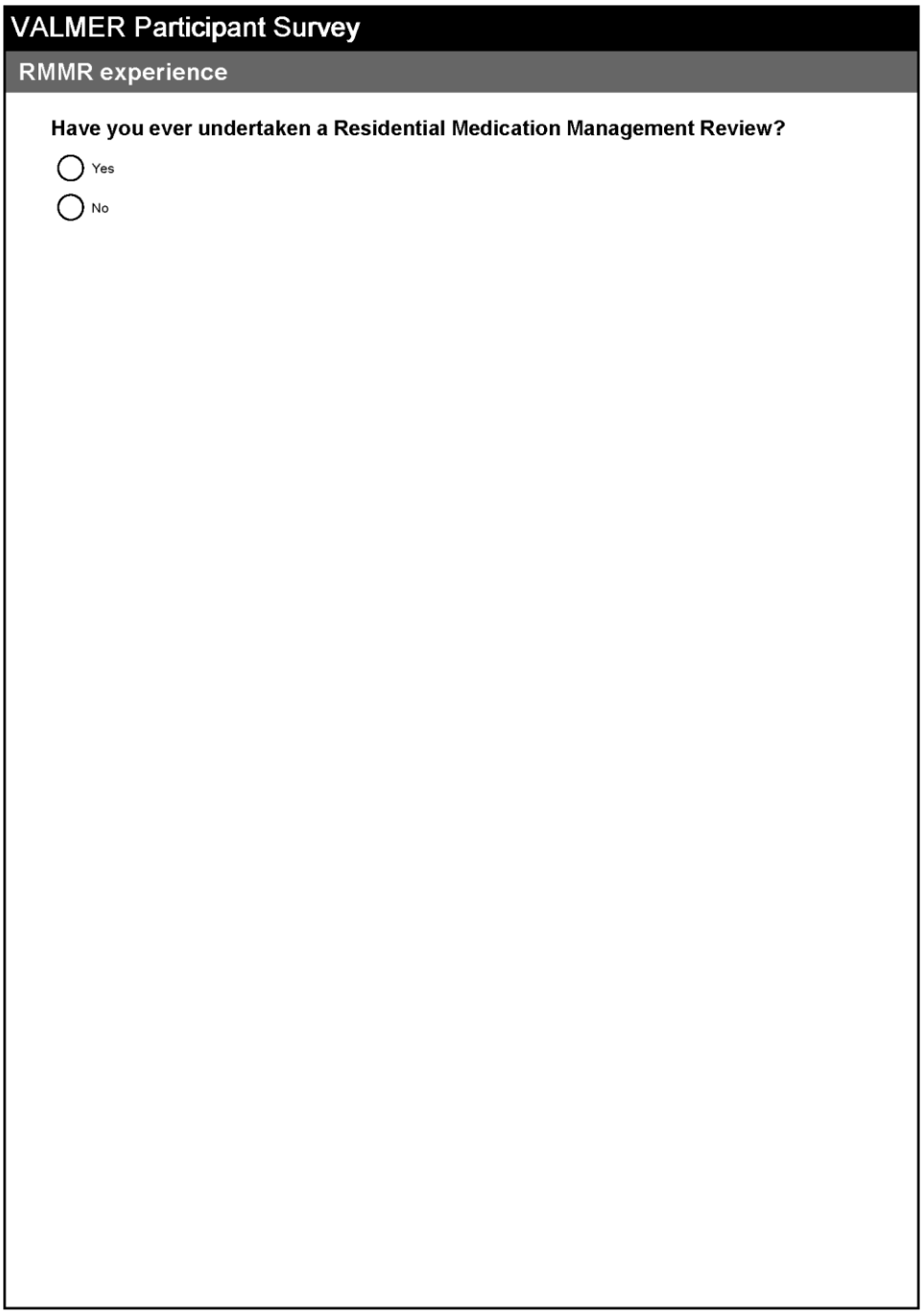

VALMER Participant Survey

RMMR experience

Have you ever undertaken a Residential Medication Management Review?

◯ Yes

◯ No

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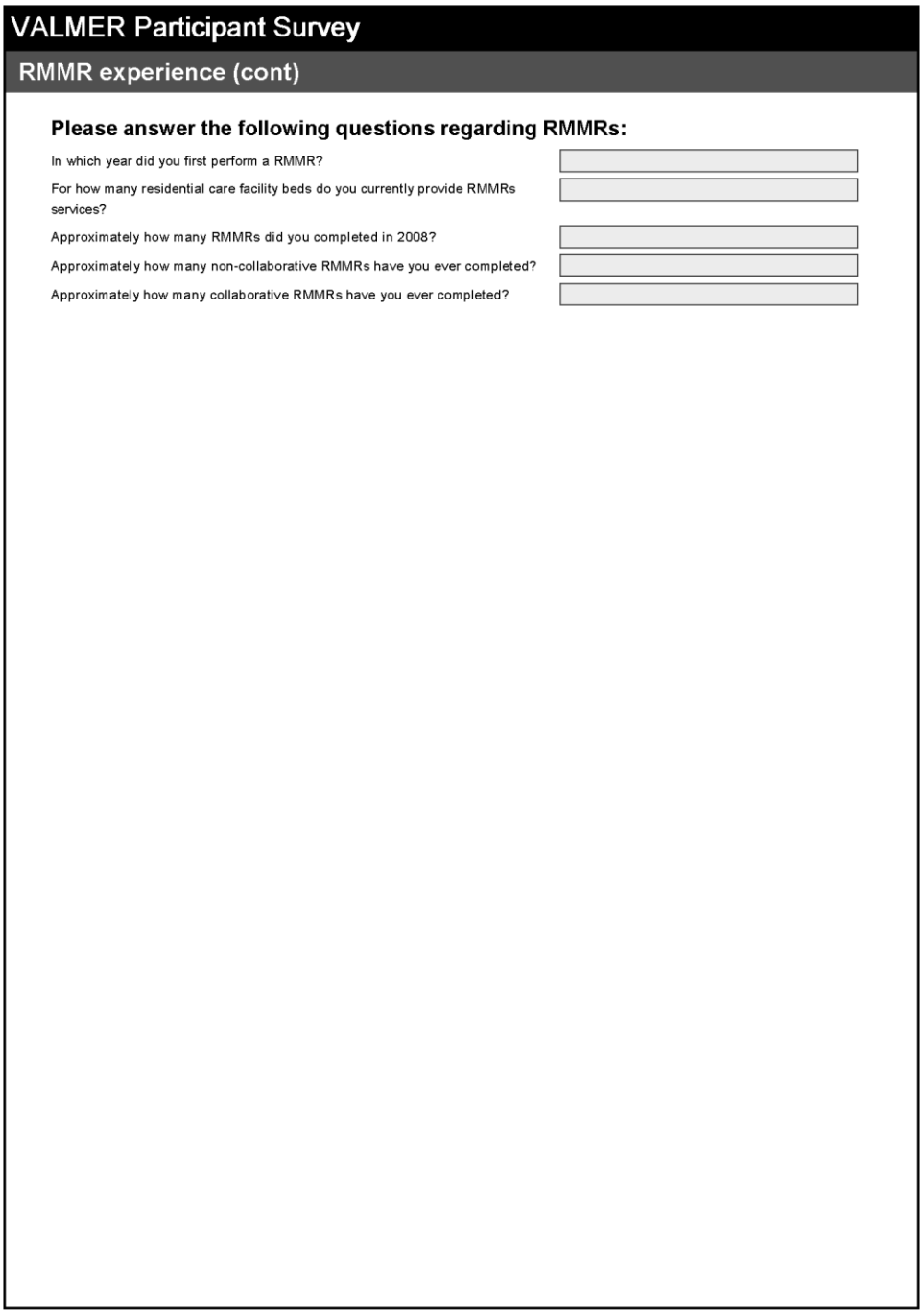

VALMER Participant Survey

RMMR experience (cont)

Please answer the following questions regarding RMMRs:

In which year did you first perform a RMMR?	
For how many residential care facility beds do you currently provide RMMRs services?	
Approximately how many RMMRs did you completed in 2008?	
Approximately how many non-collaborative RMMRs have you ever completed?	
Approximately how many collaborative RMMRs have you ever completed?	

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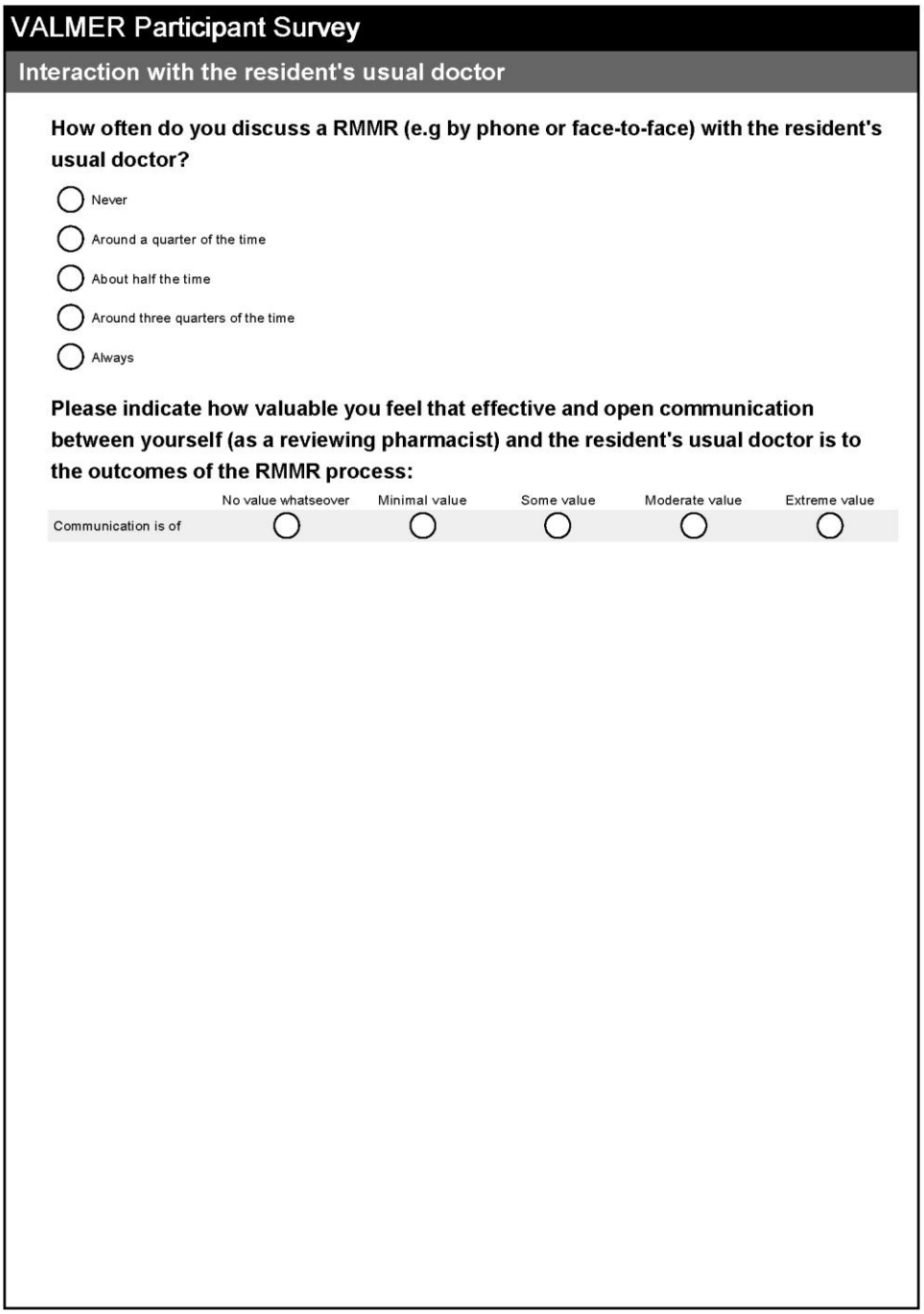

VALMER Participant Survey

Interaction with the resident's usual doctor

How often do you discuss a RMMR (e.g by phone or face-to-face) with the resident's usual doctor?

- ◯ Never
- ◯ Around a quarter of the time
- ◯ About half the time
- ◯ Around three quarters of the time
- ◯ Always

Please indicate how valuable you feel that effective and open communication between yourself (as a reviewing pharmacist) and the resident's usual doctor is to the outcomes of the RMMR process:

	No value whatseover	Minimal value	Some value	Moderate value	Extreme value
Communication is of	◯	◯	◯	◯	◯

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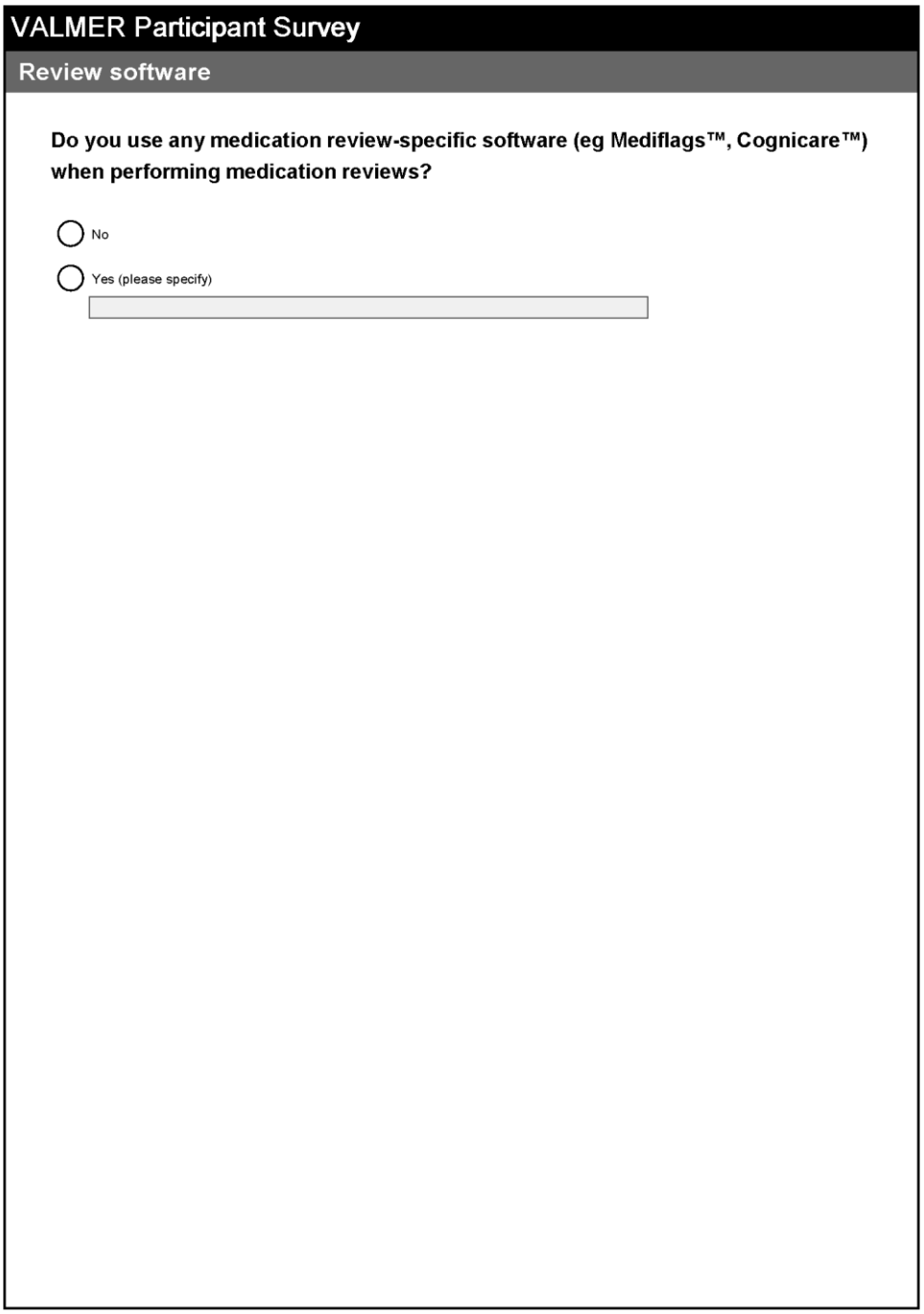

VALMER Participant Survey

Review software

Do you use any medication review-specific software (eg Mediflags™, Cognicare™) when performing medication reviews?

- ◯ No
- ◯ Yes (please specify)

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VALMER Participant Survey

Review software (cont.)

Please indicate how you utilise medication review software when performing reviews (select all that apply):

	Never	Sometimes	About half the time	Frequently	Always
Formatting reports to doctors	◯	◯	◯	◯	◯
Record keeping	◯	◯	◯	◯	◯
Identifying drug therapy problems	◯	◯	◯	◯	◯
Improving your clinical knowledge	◯	◯	◯	◯	◯

And how satisfied are you with the way that the software you are currently using performs these tasks?

	Totally unsatisfied	Somewhat unsatisfied	Neutral	Somewhat satisfied	Totally satisfied	Not applicable
Formatting reports to doctors	◯	◯	◯	◯	◯	◯
Record keeping	◯	◯	◯	◯	◯	◯
Identifying drug therapy problems	◯	◯	◯	◯	◯	◯
Improving your clinical knowledge	◯	◯	◯	◯	◯	◯

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VALMER Participant Survey

Thank you!

Your participation is greatly appreciated. The VALMER study will be completed by September 2009. Please visit www.valmer.com.au for more information and project updates.

Prize draw

Do you want to be entered into the prize draw for two bottles of Jansz wine?

◯ YES - please enter me into the draw

◯ NO - I do not want to be included in the draw

This project has been granted ethics approval by the Human Research Ethics Committee (Tasmania) Network (H9360), and is funded by the Australian Government Department of Health and Ageing as part of the Fourth Community Pharmacy Agreement through the Fourth Community Pharmacy Agreement Grants Program managed by the Pharmacy Guild of Australia.

Your privacy is important to us. The University of Tasmania's privacy policy may be viewed here

Appendix VIII - DOCUMENT classification system scope notes

D.O.C.U.M.E.N.T. FOR MEDICATION REVIEW

A CLASSIFICATION SYSTEM FOR PROBLEMS IDENTIFIED IN MEDICATION REVIEWS AND THEIR RESOLUTION

Andrew Stafford
School of Pharmacy
University of Tasmania
August 2007

TABLE OF CONTENTS

INTRODUCTION

This modified version of the D.O.C.U.M.E.N.T. system (1) has been designed to classify the drug-related problems (DRPs) identified by pharmacists in medication reviews performed in the community setting. The primary focus of this system is to allow the reconstruction of the identification and resolution of a DRP without a long-hand description of the process. It is designed to be used in conjunction with drug and disease classification systems (such as the World Health Organisation ATC and ICPC-2 PLUS systems).

The system facilitates the recording of six categories of information relating to the reviewing pharmacist's involvement in the HMR process. The categories are:

1. types and subtypes of DRPs
2. DRP identification "triggers"
3. information sources that facilitated the identification of the DRP
4. recommendations made
5. acceptance of the recommendations
6. clinical significance of the problem

Several of these categories are divided into types and subtypes. Most applications of this system will not require the user to utilise all six categories. Users may also simplify the system to their specifications by restricting their classifications to only the types of DRP and recommendation (rather than classifying to the subtype level).

This document describes how the type and subtype of each of these categories in this classification system may be used.

D.O.C.U.M.E.N.T. FOR MEDICATION REVIEW

A CLASSIFICATION SYSTEM FOR PROBLEMS IDENTIFIED IN MEDICATION REVIEWS AND THEIR RESOLUTION

1. TYPES AND SUBTYPES OF DRP

This system classifies DRPs into eight different classes of problem. Each DRP type is further sub-classified into multiple subtypes, as shown in Table 1.

	Type		Subtype	
	Code	Description	Code	Description
Type and subtype of drug-related problem	D	Drug selection	D1	Duplication
			D2	Drug interaction
			D3	Wrong drug
			D4	Inappropriate dosage form
			D5	No indication apparent
			D6	Contraindications apparent
			D0	Other drug selection problem
	O	Over or under-dose	O1	Dose too high
			O2	Dose too low
			O0	Other dose problem
	C	Compliance	C1	Taking too little
			C2	Taking too much
			C3	Intentional drug misuse
			C4	Difficulty using dosage form
			C5	Medication out of date
			C0	Other compliance problem
	U	Untreated indications	U1	Condition not adequately treated
			U2	Therapy required
			U0	Other untreated indication problem
	M	Monitoring	M1	Laboratory monitoring
			M2	Non-laboratory monitoring
			M0	Other monitoring problem
	E	Education or information	E1	Patient drug information request
			E2	Confusion about therapy
			E3	Demonstration of device
			E4	Disease management or advice
			E0	Other education or information problem
	N	Non-clinical	N1	Weight management problem
			N2	Dietary problem
			N3	Exercise problem
			N4	Smoking problem
			N5	Alcohol problem
			N6	Caffeine problem
			N0	Other non-clinical problem
	T	Toxicity or adverse reaction	T1	Toxicity caused by dose
			T2	Toxicity caused by drug interaction
			T3	Toxicity evident
			T0	Other toxicity or adverse reaction problem

Table 1 - D.O.C.U.M.E.N.T. DRP types and subtypes

The types and subtypes of DRPs are defined as follows:

Drug selection

Problems related to the choice of drug prescribed or taken by the patient

D1- Duplication

When to use:

When there are no obvious adverse clinical effects of the two drugs together, but it is either inappropriate or very unusual to see them prescribed or used together as they are from the same therapeutic class.

This also covers the specific compliance situation where a person may be inappropriately taking two brands of the same drug.

Examples of when to use:

- Patient prescribed ranitidine plus pantoprazole
- Patient prescribed Bricanyl™ and Ventolin™ inhalers
- Patient taking Aratac™ and Cordarone™ at the same time
- Patient taking Mobic™ sample provided by doctor as well as the Celebrex™ dispensed at the pharmacy

When not to use:

If the drugs involved are not of the same general therapeutic class, then use "Drug Interaction (D2)".

If the patient is experiencing adverse effects due to using the two drugs together, then use "Toxicity caused by drug interaction (T2)"

D2- Drug interaction

When to use:

When there are no obvious adverse clinical effects of the drug interaction, but the interaction is serious enough to check if the doctor knows of it.

Examples of when to use:

- patient taking tramadol and fluoxetine
- patient recently started taking amiodarone while on warfarin
- patient using an over the counter antacid when taking ketoconazole

When not to use:

If the interacting drug is of the same therapeutic class as part of the patient's existing therapy, then use "Duplication (D1)".

If the interaction is causing, or is suspected of causing a noticeable effect of any sort, then use "Toxicity caused by drug interaction (T2)".

D3- Wrong drug

When to use:

When the patient is taking a medication that has been incorrectly prescribed (prescribing error) or dispensed (dispensing error).

Examples of when to use:

- patient supplied with and taking Hydrea™ 2 m, labelled as Hydrene™ 2 m
- doctor prescribes chlorpromazine 200mg bd but intended carbamazepine 200mg bd

When not to use:

If the drug is felt to be inappropriate because of specific patient parameters such as poor renal function, then use "Contraindication apparent (D6)".

D4- Wrong dosage form

When to use:

When the formulation of the product is inappropriate or incorrect in terms of the intended use of the product.

Examples of when to use:

nystatin oral capsules prescribed to treat oral infection

ear drop product ordered or supplied for an eye problem

patient prescribed omeprazole tablets with directions to take half a tablet daily

When not to use:

If the patient has a physical problem with the administration of the dosage form as it is intended to be used (eg. swallowing a particular form of the medication whole, cannot appropriately insert suppositories, arthritis limiting the use of an inhaler) then use "Difficulty using dosage form (C4)".

If the difficulty is related to a technical problem with the use of an administration device such as an aerohaler, then use "demonstration of device (E3)".
If the difficulty is not a technical one, and related to lack of understanding of the use of the dose form, then use "Confusion about therapy (E2)".

D5- No current indication apparent

When to use:

When there is no clear apparent reason that the drug should be used.

Examples of when to use

- patient taking omperazole with no current diagnosis or symptoms of GORD
- patient using long term steroid eyedrops without a current indication

When not to use

If the drug is felt to be unnecessary due to therapeutic duplication, use "Duplication (D1)"

D6- Contraindication apparent

When to use:

When there is a contraindication or precaution to that drug being used.

When a drug or drug group is prescribed for the patient to which there has previously been a major adverse reaction.

Examples of when to use

- patient with Parkinson's disease using prochlorperazine
- patient with severe renal impairment taking metformin

When not to use

If the drug is felt to be unnecessary due to therapeutic duplication, use "Duplication (D1)".

D0- Other drug selection problem

When to use:

When a less expensive or alternative brand is available.

When there may be a more effective drug available.

Examples of when to use:

- patient's only medication is captopril taken three times daily when another once-daily ACE-inhibitor is suitable
- patient of low socioeconomic status taking Maxolon™ regularly when Pramin™ is available

Over- or under- dose prescribed

Problems related to the prescribed dose or schedule of the drug.

O1- Dose too high

When to use:

When the total daily dose of a medication prescribed is too high for the patient, either based on previous dosage or reference dose ranges.

When the dose is too high because of a particular parameter of the patient such as renal function, weight, age.

When the dose that is prescribed is too high by unintentional error.

Examples of when to use:

- patient is prescribed Diamicron™ MR 180mg in the morning
- patient is prescribed dexamethasone 50mg daily (doctor was thinking of prednisolone dose)
- patient prescribed spironolactone 100mg bd for heart failure

When not to use:

If the patient is taking too high a dose as a result of not following the appropriate directions, then use "Taking too much (C3)".

O2- Dose too low

When to use:

When the dose prescribed is either too low based on reference dose ranges or too low based on previous therapy.

This includes situations where the dose that is prescribed is too low by unintentional error.

Examples of when to use:

- locum doctor prescribes Karvea™ 150mg daily, when previous therapy was meant to be 300mg daily
- prescription for prazosin 0.5mg bd for hypertension

When not to use:

If the patient is taking a dose within the reference range to treat a condition but the condition has not adequately responded to that dose, use "Condition not adequately treated (U1)".

If the actual dose per day is suitable, but the duration is too short, then use "Other Dose problem (O0)"

If the patient is taking too low a dose of a drug as a result of not following the appropriate directions, then use "Taking too little (C1)".

O0- Other dose problem

When to use:

When the duration of use of the product is too short or too long.

When the total dose of a medication is suitable, but the frequency or the dosage schedule is inappropriate.

Examples of when to use:

- patient prescribed cephalexin 500mg qds for 3 days for cystitis.
- simvastatin ordered as 40mg in the morning
- Diamicron™ MR prescribed as three times daily

When not to use:

If the patient is not taking the appropriate dose of a product as a result of a lack of understanding of the dosage regimen, then a compliance-related code would be more appropriate.

Compliance

Problems related to the way the patient takes their medication.

C1- Taking too little

When to use:

When the patient uses too little of a medication as a result of forgetfulness or lack of understanding of the dosage regimen prescribed.

Examples of when to use:

- patient taking metformin only when-required rather than regularly
- patient using Transiderm-Nitro™ patches only every few days, not regularly
- patient not taking medication because they believe it will "stop working later on"

When not to use:

If the underuse is appropriate because of the resolution of symptoms or a condition, then use "No current indication apparent (D5)" and specify that the drug may no longer be required.

If the patient has a physical problem with the administration of the dosage form as it is intended to be used (eg. swallowing a particular form of the medication whole, cannot appropriately insert suppositories, arthritis limiting the use of an inhaler) then use "Difficulty using dosage form (C4)".

C2- Taking too much

When to use:

When the patient uses too much of a medication as a result of forgetfulness or lack of understanding of the dosage regimen prescribed.

Examples of when to use:

- patient continuing to take 50mg daily of prednisolone as they had forgotten to commence a dose reduction schedule as instructed by the doctor
- patient believes they have forgotten a medication and takes a second dose on the same day

When Not to Use:

If the overuse is due to an appropriate increase in use because of increased symptoms, then use "Condition not adequately treated (U1)"

If the overuse consists of inappropriately taking two different brands or forms of the same ingredient unknowingly, then use "Duplication (D1)".

C3- Intentional drug misuse

When to use:

When there is suspected overuse of a particular, potentially abusable, product is intentional.

Examples of when to use:

- patient dispensing history shows multiple supplies of diazepam, each of the prescriptions was written by a different doctor.

When not to use:

If the overuse is due to an appropriate increase in use because of increased symptoms, then use "Condition not adequately treated (U1)".

C4- Difficulty using dosage form

When to use:

When the patient has a physical problem with the administration of the dosage form or device as it is intended to be used (eg. swallowing a particular form of the medication whole, cannot appropriately insert suppositories, arthritis limiting the use of an inhaler).

Examples of when to use:

- patient cannot swallow their slow-release diltiazem capsules
- patient with scoliosis cannot insert suppositories
- controlled-release tablet ordered for a patient who must crush all oral medications

When not to use:

If the difficulty is related to a technical problem with the use of an administration or monitoring device such as a HandiHaler™, then use "Demonstration of device (E3)".

If the difficulty is not a technical one, and related to lack of understanding of the use of the dose form, then use "Confusion about therapy (E2)".

C5- Patient using out of date medication

When to use:

When the drug being used is expired or deteriorated in some way.

Examples of when to use:

- patient using expired Anginine™ tablets
- patient uses a monthly Dosette™ box with uncoated aspirin tablets

When not to use:

If the patient has expired medication that is not being taken, use "Other Compliance Problem (C0)".

If the patient has expired medication that they should be using but are not, use "Taking too little (C1)".

C0- Other compliance problem

When to use:

When the patient is aware of how to take the drug, is physically able to take the drug, and understands its purpose, but does not wish to take it.

When the patient unnecessarily stockpiles medication.

Examples of when to use:

- patient unwilling to use mirtazapine after reading the package insert.

When not to use:

If the compliance issue results in two drugs of the same therapeutic class being taken inadvertently, then use "Duplication (D1)".

If the patient does not wish to take the medication because it is causing an adverse event of some sort, then a toxicity or adverse event category would be appropriate.

Untreated indications

Problems relating to actual or potential conditions that require management.

U1- Condition not adequately treated

When to use:

When the patient has a symptom or disease condition that is either not being treated, or not being treated adequately.

Examples of when to use:

- patient taking Hydrene™ and Coversyl™ for high blood pressure, but blood pressure continues to be high
- patient develops nausea as part of an illness and requires addition of antinauseant medication
- patient with diabetes has a recent HbA1c of 8.2%

When not to use:

If the patient requires additional therapy as a preventative strategy (eg potassium when on a loop diuretic), then use "Preventive therapy required (U2)".

If the symptom is thought to be due to an adverse effect of a medication (such as hypertension whilst taking a high dose of venlafaxine), use "Toxicity evident (T3)".

U2- Therapy required

When to use:

When the patient requires additional therapy to prevent or treat a likely adverse event as a result of the patient's therapy, coexisting diseases, current signs/symptoms or risk factors.

Examples of when to use:

- patient commences on morphine slow release without laxative therapy
- an elderly, obese, male patient with type II diabetes and hypertension is not using antiplatelet therapy

When not to use:

If the patient already has treatment for a particular problem, but it is not sufficiently effective, use "Condition not adequately treated (U1)".

U0- Other untreated indication problem

When to use:

When the patient has any other problem relating to actual or potential conditions that requires additional management.

Monitoring

Problems relating to insufficient monitoring the efficacy or adverse effects of a drug or patient conditions in the absence of any overt adverse effects

M1- Laboratory monitoring

When to use:

When, in the absence of any adverse effects, the pharmacist believes that a laboratory test is required (e.g. potassium, creatinine, white cell count, INR).

When the pharmacist undertakes monitoring in question and provides a recommendation following the result (eg INR monitoring and suggesting a change of warfarin dose).

When, in the absence of any adverse effects, the pharmacist believes that drug level monitoring is required.

Examples of when to use:

- patient recently increased frusemide dose from 40mg daily to 120mg daily without a change in potassium replacement.
- patient commenced on amiodarone and you recommend a thyroid function test
- elderly woman on digoxin, who has not had a blood test for two years

When Not to Use:

If there are adverse effects associated with the parameter, then use "Other Toxicity problem (T0)", and specify the parameter to be tested and the symptom or sign. (eg, patient with leg cramps, suggest magnesium level).

If the need for laboratory level monitoring results from a newly commenced drug (such as a patient taking warfarin is started on fluoxetine), then use "Drug

interaction (D2)". The monitoring then becomes a recommendation, not the primary problem.

If the patient is experiencing an adverse effect of some sort, which you believe is due to elevated drug levels, then use "Caused by dose (T1)".

If the need for drug level monitoring comes about as a result of a newly commenced drug, then use "Drug interaction (D2)". The monitoring then becomes a recommendation, not the primary problem.

M2- Non-laboratory monitoring

When to use:

When, in the absence of any adverse effects, you believe that non-laboratory monitoring is required. (eg BP, BSL, temperature, weight)

Also covers the situation where the test is undertaken as a screening process.

Examples of when to use:

- a patient with heart failure has an appropriate increase in their dose of frusemide and they are advised to weigh themselves each day for the next week

When not to use:

If you recommend monitoring of a parameter (eg weight, BSL) as a result of another drug problem, then that recommendation should be recorded in the Recommendation code section. The type of problem that leads to this recommendation may vary.

M0- Other monitoring problem

When to use:

When the patient has another problem related to the monitoring of their drugs for either efficacy or adverse effects.

When the patient should be having monitoring done, but has problems with attending the laboratory, or paying for the test or equipment needed.

Education or information

Problems relating to knowledge of disease or its management

E1- Patient drug information required

When to use:

When the patient has a reasonable understanding of their condition, but requests further information about their medication.

Examples of when to use:

- patient requests information about alendronate and you provide a CMI

When not to use:

If the patient requests information primarily about the disease state, rather than a drug, then use "Disease management or advice (E4)".

If the patient does not request the information, but it is discovered that they need the information in the course of your routine dispensing, then use "Confusion about therapy (E2)".

If the request is not about a specific drug, but a therapeutic device, then use "Demonstration of device (D3)"

E2- Patient confused about therapy

When to use:

When the patient does not understand the reasons for the use of a medication, but they still take the medication as directed (ie correct dose and time).

Examples of when to use:

- when discussing metoprolol for a patient with newly diagnosed hypertension, the pharmacist finds that she believes that the drug may cure the condition and she can stop the drug in a few months

When not to use:

If the patient requests further information, then use either "Drug information request (E1)" or "Disease management or advice (E4)" as appropriate.

If the confusion would have (or did) resulted in a change in compliance (either taking too much or too little of the medication), then an appropriate compliance code should be selected.

If the request is not about a specific drug, but a therapeutic device, then use "Demonstration of device (E3)"

E3- Device demonstration

When to use:

When the patient has a technical problem with the use of an administration or monitoring device (eg inhaler, BSL Monitor, turbuhaler).

Examples of when to use:

- a patient requests a demonstration of how to use a device
- a patient is not piercing the Spiriva™ capsule in the HandiHaler™

When not to use:

If the patient understands how to use the device, but has a physical reason for not being able to use it, then use "Difficulty using dosage form (C4)".

E4- Disease management or advice

When to use:

When the primary purpose of the interaction with the patient was to inform them of critical aspects of the management or prevention of a disease or condition.

Also covers the situation where the patient requests the information, or where there is confusion about a fundamental aspect of a condition they have.

Examples of when to use:

- a patient with heart failure is counseled about fluid restriction
- information about weight loss or smoking cessation is provided for a person who has cardiovascular disease

When not to use:

If the patient request information primarily regarding a drug, then use "Drug information request (E1)".

E0- Other education or information problem

When to use:

When the prescriber is provided with information.

When any other education or information related problem is provided to the patient.

Examples of when to use:

- the pharmacist remarks that a patient with low BMD without a fracture currently taking alendronate may be eligible for PBS subsidy

Non-clinical

Problems involving aspects of patient therapy not directly related to drug therapy, such as lifestyle issues.

N1- Weight management problem

When to use:

When the patient's body weight is adversely affecting their health.

Examples of when to use:

- type II diabetic with poor glucose control with poor diet and lack of exercise
- patient with painful osteoarthritis in the knees that is exacerbated by excessive bodyweight

When not to use:

If the problem is related to measuring body weight, use "Non-laboratory monitoring (M2)".

N2- Dietary problem

When to use:

When the patient's diet is adversely affecting their health.

Examples of when to use:

- type II diabetic patient consuming excessive amounts of fat and sugar
- hypertensive patient using excessive quantities of salt
- excessive caffeine intake necessitates a patient using regular hypnotics

When not to use:

If the problem involves a dietary substance interacting with a medication, use "Drug interaction (D2)".

N3- Exercise problem

When to use:

When the patient's level of exercise is adversely affecting their health.

Examples of when to use:

- type II diabetic patient with an adequate diet but not exercising
- patient with shin-splints continues to run

When not to use:

If the problem involves a combination of diet and exercise issues, use "Weight management problem (N1)".

N4- Smoking problem

When to use:

When the patient smoking of tobacco or other substances is identified as a problem.

Examples of when to use:

- cigarette smoker with emphysema continues to smoke

N5- Alcohol problem

When to use:

When the patient's level of alcohol consumption is adversely affecting their health.

Examples of when to use:

- patient with alcoholic liver disease continues to drink large quantities of alcohol
- patient taking warfarin also drinks heavily and erratically

When not to use:

If a lack of monitoring of liver function is recommended with a patient with alcoholic cirrhosis, use "Laboratory monitoring (L1)".

N0- Other non-clinical problem

When to use:

When a patient is unable to obtain their medication due to supplier or transport issues.

When a patient is unable to afford their medication.

Examples of when to use:

- patient has erratic compliance due to lack of regular transport to the pharmacy

When not to use:

If the patient has not been obtaining their medications because they do not believe that it will work, use "Other compliance problem (C0)".

Toxicity or Adverse reaction

Problems relating to the presence of signs or symptoms which are suspected to be related to an adverse effect of the drug

T1- Toxicity caused by dose

When to use:

When the patient has signs or symptoms that suggest an adverse reaction that is likely to be dose related.

Where compliance issues have lead to symptoms of toxicity.

Examples of when to use:

- patient has increased their dose of tramadol and develops headache, sweating and agitation
- patient prescribed Diamicron™ MR 90mg daily and has significant hypoglycaemic symptoms
- patient intentionally misusing medication presents with signs or symptoms of toxicity

When not to use:

If the patient does not have any signs or symptoms of adverse effects and you believe the dose is too high, then use "Dose too high (O1)"

T2- Toxicity caused by drug interaction

When to use:

When the patient has signs or symptoms that suggest an adverse reaction that relates to the presence of an interacting drug

Examples of when to use:

- patient taking warfarin develops an elevated INR after commencing metronidazole
- patient taking perindopril and frusemide, who commences diclofenac and develops renal dysfunction
- promethazine and amitriptyline together causing dry mouth

When not to use:

If the patient has an interacting drug present, but there are NO signs or symptoms of the interaction causing an adverse effect, then use "Drug interaction (D2)".

Where the patient has been prescribed interacting drugs but has not taken the medications.

T3- Toxicity evident

When to use

When there are symptoms of toxicity but the cause is not due to interaction or dose, but there is a suspected medication cause.

Examples of when to use

- patient on captopril develops a dry cough.

When not to use

If there are no signs or symptoms of toxicity or adverse reaction.

T0- Other toxicity problem

When to use:

When the patient has signs or symptoms that suggest an adverse reaction that is likely to be related to a particular drug, but doesn't seem to be dose related or related to an interaction.

Examples of when to use:

- patient develops hypotension after commencing prazosin, even though the dose is controlling the prostatic hypertrophy

When not to use:

If there are no signs or symptoms of adverse effects.

2. DRP IDENTIFICATION "TRIGGERS"

This classifies what information prompted the identification the DRP. Multiple triggers are possible for each problem identified.

The use of this system is best illustrated using examples. For example, metformin is recognised as potentially causing the adverse effect of lactic acidosis in patients with poor renal function. Many patients taking metformin, however, have adequate renal function and are not at risk of lactic acidosis. Hence, if a patient with renal failure was taking metformin, it is assumed that a pharmacist would identify the patient as being at risk of a DRP. Conversely, the pharmacist would not identify a patient with adequate renal function as being at risk of the same DRP. The DRP identified would therefore be considered as resulting from at least two triggers, one concerning the drug and the other the patient.

Not all DRPs would require two or more triggers to identify them. Hydroxychloroquine is associated with the development of retinal changes which may impair vision. No conditions have been identified which may put a patient at risk of this adverse effect, and it is recommended that patients taking hydroxychloroquine have their vision examined regularly. A pharmacist may thus identify hydroxychloroquine as a cause of a potential monitoring DRP solely with the knowledge that the patient is taking it.

Table 2 shows the DRP trigger types and subtypes:

	Type		Subtype	
	Code	Description	Code	Description
Identification trigger	D	Drug	D1	Direct drug action
			D2	Indirect drug action
			D3	Pharmacokinetic parameters
			D4	Other drug factors
	O	Observations and monitoring	O1	Urea, electrolytes, LFTs
			O2	Patient observations
			O3	Organ specific pathology
			O4	Haematology pathology
			O5	Other pathology
	P	Patient	P1	Medical conditions
			P2	Knowledge and understanding
			P3	Compliance

Table 2 - DRP trigger types and subtypes

Drug factors

When knowledge of the drug/s characteristics is used in the identification of the DRP.

D1- Direct drug action

When to use:

When the DRP results from the direct desired actions of the drug.

Examples of when to use:

- patient with postural hypotension induced by prazosin ("Medical conditions (P1)" would also apply)
- patient suffering regular hypoglycaemia due to insulin administration too soon before a meal (Knowledge and understanding (P2) may also apply)

D2- Indirect drug action

When to use:

When the DRP results from the indirect or undesired actions of the drug, such as adverse effects.

Examples of when to use:

- patient taking tamoxifen suffers from hot flushes ("Medical condition (P1)" would also apply)

D3- Pharmacokinetic parameters

When to use:

When the DRP results from the pharmacokinetic parameters of the drug.

Examples of when to use:

- patient taking diltiazem is also prescribed cyclosporine

D4- Other drug factors

When to use:

When the DRP results from a parameter of the drug not fitting into the above categories, such as supply issues or cost issues.

Examples of when to use:

- patient taking vitamin D and alendronate is recommended a combination product

Patient factors

When knowledge of the patient's characteristics is used in the identification of the DRP.

P1- Medical conditions

When to use:

When the DRP is identified from the medical conditions of the patient.

Examples of when to use:

- patient with Type II diabetes and family history of ischaemic heart disease not taking an antiplatelet agent
- patient with an intractable cough takes an ACE inhibitor (Indirect drug action (D2) would also apply))

P2- Knowledge and understanding

When to Use:

When the DRP is identified from a deficiency in the patient's knowledge or understanding of their conditions or medications.

Examples of when to use:

- patient with Type II diabetes believes that their medications will substitute for diet and exercise
- patient taking alendronate with an iron supplement as they are unaware of the correct administration procedure

P3- Compliance

When to Use:

When the DRP results from the patient's non-compliance (intentional or unintentional) with their medical regimen.

Examples of when to use:

- patient with asthma using only a reliever and not their preventer because of an aversion to steroid therapy
- patient's dispensing history shows multiple missed doses of various medications

Observations and monitoring

When the result of measurement/s of patient parameters are used in the identification of the DRP.

O1- Urea and electrolytes

When to use:

When the DRP is identified from U&E pathology.

Examples of when to use:

- patient taking spironolactone and fosinopril has a high potassium level ("Indirect drug action (D2)" would also apply)

O2- Patient observations

When to Use:

When the DRP is identified from observations.

Examples of when to use:

- patient taking indapamide has high blood pressure ("Medical conditions (P1)" would also apply)
- patient with diabetes is overweight ("Medical conditions (P1)" would also apply)

O3- Organ specific pathology

When to use:

When the DRP is identified from organ-specific pathology.

Examples of when to use:

- patient has a low T_4 and high TSH ("Medical conditions (P1)" would also apply)
- patient taking a statin has elevated creatine kinsase and LFTs ("Indirect drug action (D2)" would also apply)

O4- Haematology pathology

When to use:

When the DRP is identified from haematology pathology.

Examples of when to use:

- patient taking metformin has a low vitamin B_{12} level ("Indirect drug action (D2)" would also apply)

O5- Other pathology

When to use:

When the DRP is identified from pathology not otherwise categorised.

Examples of when to use:

- trimethoprim resistance shown in patient taking trimethoprim for UTI prophylaxis

3. INFORMATION SOURCES

This classifies where the information that triggered the identification of the DRP was sourced. Multiple sources are possible for each DRP trigger used. The DRP trigger sources defined in this system are shown in Table 3, and detailed below.

	Type
Code	Description
I1	Referral
I2	Patient interview
I3	Patient notes
I4	Non-patient discussion
I5	Dispensing history

Table 3 - DRP trigger sources

I1- Referral

Referral information includes the patient information supplied in the GP's referral to the pharmacist. It may include past and present diagnoses, a medication list, patient age, height, weight etc. It is not considered to contain care notes.

When to use:

When the pharmacist used the information contained within the referral to identify the problem.

When the pharmacist used the information related to monitoring (laboratory or non-laboratory) to identify the problem.

Examples of when to use:

- drug interactions identified from the patient's medication list
- ACE inhibitor induced hyperkalaemia confirmed by pathology results

I2- Patient interview

When to use:

When the pharmacist used the information obtained via the patient interview to identify the problem.

Examples of when to use:

- compliance issues or adverse effects identified from discussion with patient.
- pharmacist identifies consistently high morning blood sugar levels from the patient's blood glucose monitor

I3- Patient notes

When to use:

When the pharmacist uses the information contained within patient case notes to identify the problem.

Examples of when to use:

- the patient notes contain information that facilitates the identification of an adverse effect

I4- Non-patient discussion

When to use:

When the pharmacist used the information obtained via interviewing a carer, nursing staff or associate of the patient to identify the problem.

Examples of when to use:

- adverse drug effect identified from discussion with nursing staff at an Aged Care Facility

When not to use:

If the problem was identified from discussion with the patient, use "Patient interview (I3)".

I5- Dispensing history

When to use:

When the pharmacist used the information obtained from the patient's dispensing history to identify the problem.

Examples of when to use:

- patient claims to be using medications as prescribed, however dispensing history shows inconsistent dispensings

4. RECOMMENDATIONS MADE

What the pharmacist recommended to resolve a DRP. Multiple recommendations are possible for each DRP identified.

Absence of a recommendation

When no recommendation is made regarding an identified DRP.

A1- No recommendation necessary

When to use:

When a DRP is identified that requires no involvement from the prescriber, or is resolved by the reviewing pharmacist at the time of review.

Examples of when to use:

- patient not using inhaler correctly, and pharmacist corrected inhaler technique at the time of the review

When not to use:

If the action requires follow-up after the intervention, use "Follow-up (F1) or (F2) as appropriate".

A2- No recommendation made

When to use:

When the pharmacist identifies a DRP but does not make a recommendation to resolve it.

Examples of when to use:

- the pharmacist notes that a patient's potassium levels have steadily increased over the last three set of pathology results, but does not suggest reducing their perindopril dose

When not to use:

If a recommendation is not required, use "No recommendation necessary (A1)".

Drug therapy change

When the pharmacist recommends a change to the patient's drug therapy.

D1- Dose increase

When to use:

When the pharmacist recommends increasing the dose of a medication.

Examples of when to use:

- the pharmacist notes that a patient is hypertensive, and suggests an increase in amlodipine dose

When not to use:

If the pharmacist recommends to change one drug to a combination product, use "Drug switch (D7)".

D2- Dose decrease

When to use:

When the pharmacist recommends decreasing the dose of a medication.

Examples of when to use:

- the pharmacist notes that a patient is has poor renal function, and suggests a decrease in allopurinol dose

D3- Drug cease

When to use:

When the pharmacist recommends to cease a medication.

Examples of when to use:

- the pharmacist notes that a patient is taking both ranitidine and omeprazole, and recommends to cease the ranitidine

When not to use:

If the pharmacist recommends to change two drugs to a combination product, use "Formulation change (D5)".

D4- Drug start

When to use:

When the pharmacist recommends that the patient be initiated on a new medication.

Examples of when to use:

- a type II diabetic is recommended to be commenced on aspirin to reduce cardiovascular risk

When not to use:

When a drug is suggested to be started in place of another drug to be ceased, use "Drug switch (D7)".

D5- Formulation change

When to use:

When the active ingredient of the medication and its total daily dose is not changed, but the formulation is changed.

When the pharmacist recommends changing to a combination product containing the same dose of two drugs currently taken.

Examples of when to use:

- pharmacist suggests a change from a metered dose inhaler to an autohaler
- pharmacist suggests a change from Norvasc™ 5mg and Lipitor™ 20mg to Caduet™ 20/5mg
- the pharmacist suggests a change from cream to ointment as the cream is not available

When not to use:

If the formulation change also results in a change in the total daily dose of the medication, then use "Dose increase (D1)" or "Dose decrease (D2)" where appropriate.

If the change also results in a change in one or both of the drugs taken, such as Zanidip™ 10mg and Lipitor™ 20mg to Caduet™ 20/5mg, use "Drug switch (D7)".

D6- Dose schedule change

When to use:

When the total daily dose of the product remains the same, but the pharmacist suggests a change in the number of times a day, or the timing of the doses each day.

Examples of when to use:

- pharmacist suggests changing valproate from 1g twice daily to 500mg four times daily to reduce gastric upset
- pharmacist suggests a change in timing of isosorbide mononitrate from morning to night to cover unstable angina during the night

When not to use:

When the change results in a change in the total daily dose of the medication, use "Dose change (R1)"

D7- Drug switch

When to use:

When the pharmacist recommends replacing one drug with another.

Examples of when to use:

- patient describes ongoing drowsiness in the mornings with night-time nitrazepam, and the pharmacist suggests a change to temazepam

When not to use:

If the recommendation involves switching from two drugs to a combination product, use "Drug switch (D7)".

D8- Other drug therapy change

When to use:

When the pharmacist makes a recommendation regarding drug therapy that cannot be otherwise classified.

Education

When the pharmacist provides written or verbal education to resolve an identified DRP.

E1- Patient education

When to use:

When the pharmacist conducts a detailed counselling or education session with the patient or carer that is specifically targeted at resolving the problem that has been identified.

Examples of when to use:

- patient was not taking metformin correctly, pharmacist gave details of how to take it in relation to food, how long it lasts and also gave information regarding the complications and management of diabetes

When not to use:

If the discussion with the patient is only to determine the nature of the problem, rather than propose a resolution recommendation or further education, then it is an investigative action only. A conversation or discussion with the patient may involve both investigation of the problem (see "Factors leading to identification of the Problem" above) and an education/counselling session to resolve the problem identified- use "Patient education (E1)".

E2- Prescriber information

When to use:

When the pharmacist provides information to the prescriber that resolves a DRP.

Examples of when to use:

- patient with osteoporosis without a fracture is supposed to take alendronate as treatment but cannot afford it. The pharmacist informs the prescriber that the patient may now be eligible for government subsidy

When not to use:

If the pharmacist identifies a problem but makes recommendations to the prescriber which require further investigation, use "Follow-up by prescriber (F1)".

E3- Compliance assistance

When to use:

When the pharmacist provides the patient with a detailed list of their medications such as a Medipal™ or Medprof™, or one of their own format.

When the pharmacist suggests the use of a dose administration aid such as a Dosette™ box or a Webster-pack™.

Examples of when to use:

- a patient with identified poor compliance is recommended to commence a Webster-pack™

When not to use:

When the pharmacist identifies poor compliance as an issue but makes no recommendation on how to resolve the issue, use "No recommendation made (A2)".

Follow-up

When an actual or potential DRP is identified, but the pharmacist makes a recommendation of further investigation that is not related to monitoring to resolve it.

F1- Follow-up by prescriber

When to use:

When an actual or potential DRP is identified, but the pharmacist refers the patient back to the prescriber for further investigation.

Examples of when to use:

- a patient is documented has having had only one pneumococcal vaccination and the pharmacist recommends that the doctor investigate the patient's vaccination status and rectify if appropriate

When not to use:

If the pharmacist identifies a problem but makes no recommendations to the prescriber which suggest that further investigation is required, use "No recommendation made (A2)".

F2- Follow-up by another

When to use:

When an actual or potential DRP is identified, but the pharmacist refers the patient to another health professional for further investigation.

Examples of when to use:

- a diabetic with poor diet is recommended to visit a dietician for dietary advice
- a patient with poor eyesight is referred to an optometrist for an eyesight check

When not to use:

If the pharmacist identifies a problem but makes no recommendations that another health professional should be involved for further investigation, use "No recommendation made (A2)".

Monitoring

When the pharmacist recommends that additional monitoring be performed to ensure therapeutic efficacy or exclude potential adverse effects.

S1- Laboratory monitoring

When to use:

When the pharmacist suggests to the prescriber that they undertake some laboratory monitoring for efficacy or adverse medication effects.

Examples of when to use:

- the pharmacist suggests that they check the potassium level of a patient taking spironolactone and trandolapril
- the pharmacist suggests a phenytoin level be performed

When not to use:

If the monitoring relates to a test that can be done at home (eg BSL) then use "Non-laboratory monitoring (S2)".

S2- Non-laboratory monitoring

When to use:

When the pharmacist suggests that the patient undertake some non-laboratory monitoring for efficacy or adverse effects from the medication.

Examples of when to use:

- the pharmacist suggests the patient weigh themselves daily while they are taking an increased dose of frusemide for heart failure

When not to use:

If the monitoring involves laboratory-based test of some sort, then use "Laboratory monitoring (S1)".

5. ACCEPTANCE OF THE RECOMMENDATIONS

Did the clinical activity actually result in a change of management, or was the suggestion deemed not relevant in this case? In certain circumstances, a pharmacist may offer multiple ways to resolve to the one DRP, and it is not necessary for all of the recommendations made to be accepted to resolve the DRP.

Totally accepted

When to use:

When the recommendation(s) that the pharmacist makes to resolve a DRP are totally accepted by the prescriber and the suggested changes are implemented in full.

Examples of when to use:

- the pharmacist identifies a patient as having diarrhoea due to metformin, and recommends reducing the metformin dose and introducing glimepiride. The prescriber accepts both recommendations

When not to use:

If only certain recommendations are accepted, use "Partially accepted".

Partially Accepted

When to use:

When the pharmacist makes multiple recommendations, and only some of the recommendations that were made are accepted by the prescriber.

Examples of when to use:

- the pharmacist recommends a reduction of the dose of digoxin and a repeat blood level of digoxin. The prescriber agrees with the reduction in dose, but the blood level would be unnecessary

When not to use:

If all of the recommendations are accepted, use "Accepted".

Not accepted

When to use:

When all of the recommendation(s) that the pharmacist makes are rejected.

Examples of when to use

- the pharmacist recommends cessation of tramadol and a trial of paracetamol; the prescriber continues the tramadol as paracetamol was ineffective for the patient in the past

When not to use:

- If the prescriber makes changes to resolve the DRP that were not suggested by the pharmacist, use "Alternative resolution".

Alternative resolution

When to use:

When the prescriber rejects the recommendations made by the pharmacist but makes changes to resolve the DRP in an alternative way.

Examples of when to use

- the pharmacist recommends adding a proton-pump inhibitor to reduce the risk of gastrointestinal bleeding in a patient taking diclofenac; instead, the prescriber changes the diclofenac to oxycodone and does not commence a proton pump inhibitor.

6. CLINICAL SIGNIFICANCE OF THE PROBLEM

If the pharmacist had not intervened/provided a clinical activity, what was the possible/potential outcome if therapy had continued?

This is a subjective rating which predicts the clinical severity if action was not taken.

That is: How serious was/could have been the problem?

Note 1: Situations rated as high (S4) will require additional information to be entered into a notes field

S0- Nil significance

When to use:

When there is no consequence to the patient and no change in their management. No further investigation or follow-up by the prescriber or patient is necessary.

Examples of when to use:

- the pharmacist notes an interaction that is of no clinical consequence to the patient

When not to use:

If the DRP requires any further monitoring or investigation then significance should be at least "Low significance (S1)".

S1- Low significance

When to Use:

When the consequence to the patient are related to costs or information only.

When drug regimens are simplified by the recommendation of combination products.

Examples of when to use:

- provided CMI or Self Care card
- lifestyle advice given
- patient taking Norvasc™ and Lipitor™ is recommended to be prescribed Caduet™

S2- Minor significance

When to Use:

When the consequences to the patient are that they have improved a minor symptom, or if the intervention had not occurred they would have developed a minor symptom.

When the DRP identified attributes potential adverse drug effects to a medication/group of medications without substantial evidence that the medication/s are the cause of the adverse effect.

The DRP should be either resolved at the time of the review by the pharmacist without directly involving the doctor, or not require a significant change in prescribing.

Examples of when to use:

- poor compliance results in the pharmacist recommending a Webster pack™
- pharmacist tells a patient to take pravastatin at night for improved efficacy
- pharmacist suggests checking renal function in absence of symptoms of digoxin toxicity
- pharmacist recommends influenza or pneumococcal vaccination

S3- Moderate significance

When to Use:

When the DRP identified requires significant management by the patient's prescriber.

When the problem is a minor but overt adverse effect that is more than likely caused by a drug or interaction.

Examples of when to use:

- patient experiencing a cough attributable to their ACE inhibitor
- morning ataxia due to combination of night-time doses of amitriptyline and temazepam

S4- High significance

When to Use:

When the DRP identified was likely to result in the patient having to go to a hospital because of the consequences.

When if the intervention did not occur, it was likely the patient would have had to receive assistance from a regular nurse visit, or would have had to been placed into residential care of some sort.

When the intervention prevents additional nursing care or delays the admission into residential care.

When the problem is an actual severe adverse effect that is more than likely caused by a drug or interaction.

Examples of when to use:

- a patient on lithium recently prescribed an NSAID complained of increased tremor and diarrhoea. The pharmacist recommended immediately ceasing the NSAID and checking the lithium level

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1. Peterson G, Tenni P. Identifying, prioritising and documenting drug-related problems. Australian Pharmacist 2004;23(10):706-9.

2. van Mil JW, Westerlund LO, Hersberger KE, Schaefer MA. Drug-related problem classification systems. Ann Pharmacother 2004;38(5):859-67.

Appendix IX has been removed for copyright or proprietary reasons

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Appendix X - Advertisement for recruitment of specialists for HMR assessment

VALMER AACP UTAS
The Value of Home Medicines Reviews

UMORE
School of Pharmacy
University of Tasmania
Private Bag 26
Hobart Tasmania 7001

19 November 2008

Dear Doctor

Re: VALMER study (the Value of Home Medicines Reviews)

The School of Pharmacy at the University of Tasmania is currently undertaking research into the outcomes of medication reviews performed by pharmacists for patients living at home. In a study entitled VALMER (the Value of Home Medicines Reviews), virtual panels of "medication-therapy experts" will be asked to provide opinions as to the probable outcomes of the recommendations made by pharmacists in these reviews.

We are seeking expressions of interest from general physicians who may wish to participate in these virtual panels. Participants will provide their opinions using an internet-based system that may be accessed from any location with internet access. Participation will involve a time commitment of approximately 20 hours that may be performed at any time between January and March 2009. Participants will receive approximately $150/hour for their time.

For more information regarding the study, please contact either Peter Tenni (pctenni@utas.edu.au) or Andrew Stafford (andrews5@utas.edu.au) at the University of Tasmania, or call 03 6226 1715. More information may also be found at the project website www.valmer.com.au.

Yours sincerely

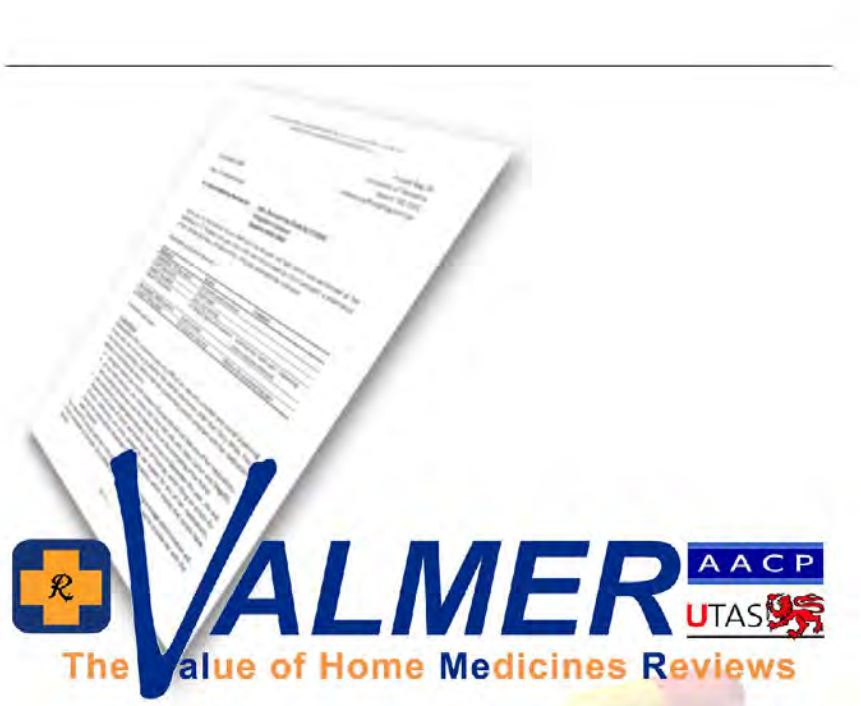
Dr. Peter Tenni
Chief Investigator

Professor Greg Peterson
Co-Investigator

Andrew Stafford
Project pharmacist

This project has been granted ethics approval by the Human Research Ethics Committee (Tasmania) Network (H9360), and is funded by the Australian Government Department of Health and Ageing as part of the Fourth Community Pharmacy Agreement through the Fourth Community Pharmacy Agreement Grants Program managed by the Pharmacy Guild of Australia.

Appendix XI - Training manual for HMR assessment



VALMER

HMR Assessment System

User Guide

This study is funded by the Australian Government Department of Health and Ageing as part of the Fourth Community Pharmacy Agreement

Table of Contents

1. Introduction

The VALMER (Value of Medication Reviews) study is an 18-month project conducted by the Unit for Medication Outcomes Research and Education, School of Pharmacy, University of Tasmania, with collaborators from the Australian Association of Consultant Pharmacy and the University of New South Wales. The project aims to address a relative lack of research into Home Medicines Reviews (HMRs) by evaluating the outcomes of a sample of medication reviews to determine the cost-effectiveness of the HMR program.

The VALMER study uses a predictive economic modelling technique to assess the outcomes of HMRs rather than a randomised control (RCT) design. The primary reason for this design is to permit a more comprehensive analysis of individual HMRs than a RCT would allow (within the constraints of the VALMER budget). Several prior studies of pharmacist-conducted medication reviews have identified that the benefits of these reviews are primarily a reduction in the number of medications taken and improved patient medication knowledge. Current evidence suggests that medication review does not reduce hospitalisations or mortality, and does not significantly improve quality of life. By modelling the outcomes of HMRs, data from the VALMER study may also be used to improve the HMR process and subsequently patient outcomes.

The VALMER study uses expert medical opinion to model the outcomes of HMRs via an online system. Several experts (including specialist physicians, clinical pharmacologists, general practitioners and clinical pharmacists) assess each HMR to generate a consensus opinion as to the likely outcomes of that HMR. This document provides an overview of the HMR assessment process and describes how to use the online system.

2. Nature of the assessment

A HMR involves a specially-accredited pharmacist formally reviewing a patient's medication and their management of it upon receiving a referral from the patient's general practitioner. Following an interview with the patient, the pharmacist formulates a report that documents any problems relating to the patient's medication management, as well as recommendations to resolve these issues. This report is forwarded to the general practitioner who addresses the issues raised in the HMR (if they consider them to be appropriate).

The VALMER study methodology assumes that each HMR consists of several smaller interventions that address individual drug-related problems; for example, commencing one medication, ceasing another, or performing some therapeutic drug monitoring. Associated with most of these smaller interventions are numerous potential "consequences"- these consequences may be either beneficial or detrimental to a patient's health. Ideally, the net effect of all the consequences associated with each intervention will be positive, resulting in the HMR benefiting a patient's health.

For the VALMER study, a standard list of 52 potential consequences has been formulated. There are three levels of severity for each consequence, termed "mild", "moderate" and "severe", and each severity level is described by a short vignette. Two example consequences are shown in Table 2.1. In previous studies undertaken at the University of Tasmania, each consequence has been linked to several health outcomes, including GP and specialist visits, hospitalisation, and quality of life.

Consequence Severity level	Description
Hypertension	
• **Mild**	Mild signs or symptoms of hypertension which resolve without intervention
• **Moderate**	Moderate elevation of blood pressure requiring modification of or commencement of medical management
• **Severe**	Hypertension resulting in acute injury to target organs (e.g. renal, ocular or cerebral) requiring prompt medical management
Hyperkalaemia	
• **Mild**	Mild signs or symptoms of hyperkalaemia which resolve without intervention
• **Moderate**	Hyperkalaemia requiring medical management and/or modification of medication regimen
• **Severe**	Hyperkalaemia requiring prompt medical management and investigation (e.g. palpitations, bradycardia)

Table 2.1 - Example consequences

The complete list of consequences may be found at the end of this document (Appendix I).

The VALMER assessment process involves choosing appropriate consequences (both positive and negative) for each intervention, and assigning a likelihood of them occurring in a particular patient as a result of that intervention. A positive effect (i.e. a benefit on a patient's health) is indicated by a reduction in the probability of a consequence occurring; detrimental effects occur when the probability of a consequence increases.

For example, consider the following scenario:

- A patient with chronic atrial fibrillation is taking aspirin to prevent thromboembolism. In a HMR, the pharmacist recommends changing the aspirin to warfarin.

There are several potential consequences that may be associated with this intervention, two of which are cerebrovascular ischaemia and bleeding. Prior to the HMR (this can be termed the BEFORE scenario), the patient would be at a certain level of risk of both of these consequences. Assuming that aspirin is changed to warfarin (the AFTER scenario), these risks will change - the risk of a CVA may decrease, but the risk of bleeding may increase. In both cases, the probability of each consequence occurring at different severity levels may also be different. In the above example, it is likely that the probability of minor bleeding occurring will be much higher than the risk of major bleeding. Table 2.2 presents a conceptual representation of this example.

CONSEQUENCE	SEVERITY LEVEL	PROBABILITY OF CONSEQUENCE OCCURRING	
		BEFORE INTERVENTION	AFTER INTERVENTION
Bleeding	**Mild**	A_1	$A_1 + X_1$
	Moderate	A_2	$A_2 + X_2$
	Severe	A_3	$A_3 + X_3$
Cerebrovascular event	**Mild**	B_1	$B_1 - Y_1$
	Moderate	B_2	$B_2 - Y_2$
	Severe	B_3	$B_3 - Y_3$

Where A_i = probability of consequence A occurring at i level of severity
B_i = probability of consequence B occurring at i level of severity
X_i = change in probability of consequence A occurring at i level of severity
Y_i = change in probability of consequence B occurring at i level of severity

Table 2.2- Hypothetical example of consequences due to a HMR

The VALMER system is designed to utilise your knowledge of evidence-based medicine and your clinical experience to predict consequences and assign probabilities of them occurring at each severity level for interventions made in HMRs. By selecting appropriate consequences for each scenario, and assigning probabilities to each severity level of each consequence occurring, we hope to predict the outcomes of HMRs on patient health. Your evaluation of HMRs in this way will provide invaluable information regarding medication reviews, and potentially provide guidance toward improving the HMR process and ultimately patient outcomes.

3. Using the system

The process of assessing a HMR using the VALMER system is summarised in Figure 3.1.

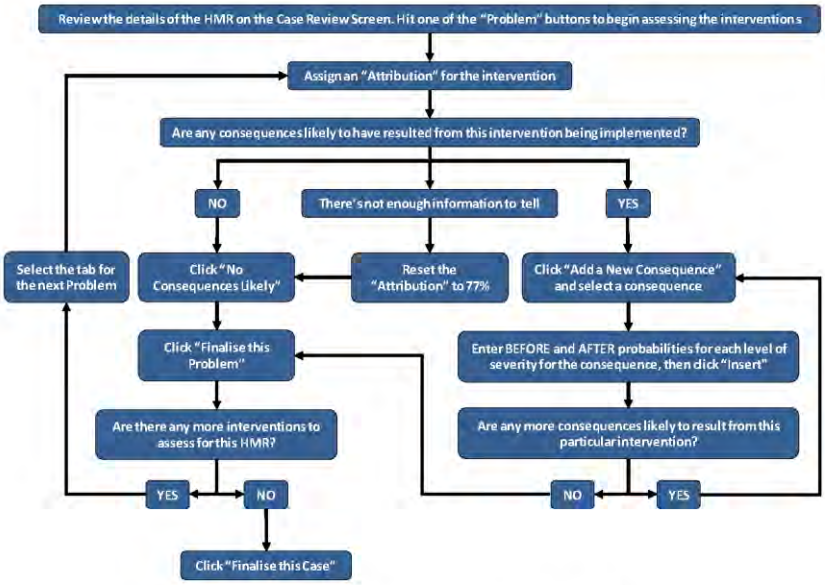


Figure 3.1 - Flowchart for HMR assessment in the VALMER system

3.1 Core assumptions

When using the VALMER online assessment system, the following assumptions and considerations should be made:

- You are asked to predict the outcome of each intervention, *assuming that each recommendation was actually implemented*.
- The time horizon for the study is 12 months, hence you are asked to estimate the likelihood of the chosen consequence occurring *in the next 12 months*.
- The date of the HMR does not be taken into consideration if clinical guidelines have changed since due to new evidence.
- As the pharmacist is only one member of a patient's health-care team, it is possible that another party may identify the same problem and resolve it. You will also be asked to provide an estimate of "attribution" for each intervention, which is the likelihood that the intervention resulted only from the actions of the pharmacist who performed this HMR.
- It is possible (and probable) that some of the problems identified or recommendations made will be inappropriate for the patient. You are not required to explicitly identify inappropriate recommendations; this will be evident from your selection of consequences.

- Each problem should be assessed independently of the others in each case; i.e. the consequences selected for one drug-related problem and its resolution/s do not affect the consequences of the recommendations made to resolve the other drug-related problems in the HMR.
- There is no limit to the number of consequences that may be selected for each recommendation. However the likelihood of many of them occurring will be extremely small, hence you may wish to restrict the consequences you select to those most likely to occur in each scenario.
- A **positive** effect (i.e. a benefit on a patient's health) is indicated by a **reduction** in the probability of a consequence occurring; **detrimental** effects occur when the probability of a consequence **increases**.
- Many recommendations will be unlikely to have any effect on a patient's health at all (that is, they will be of no consequence).
- Unfortunately, many cases provide very limited information regarding the patient. This will require you to make several assumptions about the patient. If there is simply not enough information to make any judgement about the case, an "Insufficient information" option is available (see Section 3.2.3), but should be used sparingly.

The following section describes in detail how to use the VALMER online assessment system.

3.2 How to use the system

3.2.1 Case (HMR) Management

Log on to the system using the username and password that has been provided to you. Once logged on, you are presented with the **Case Management Screen** (Figure 3.2). At this screen, users can view details about the cases (HMRs) that have not been assessed, as well as those they have completed. Ten cases are shown on this screen; to view the next ten, click the "Next" link.

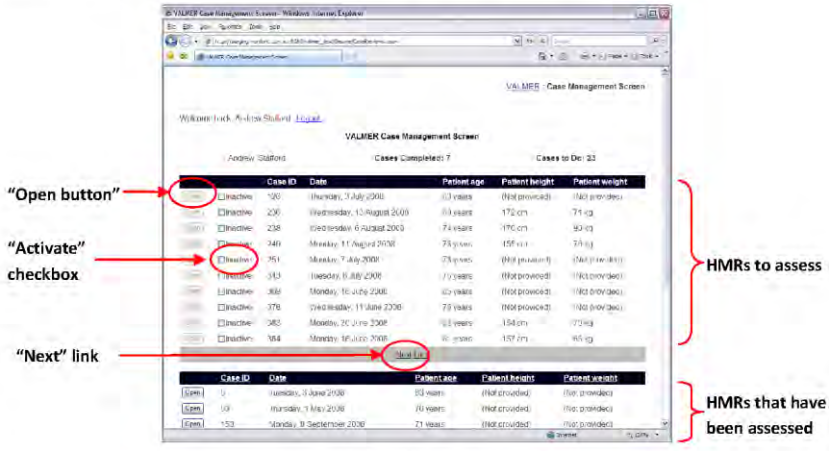


Figure 3.2 - Case Management Screen

By default, all HMRs that have not yet been assessed are "Inactive"- to make a HMR "Active", tick the checkbox to the left of the "Case ID". Several HMRs may be active at any one time, which is useful if you wish to work on several cases at once or browse through the remaining HMRs. Once a case has been made "Active", the "Open button" beside the check box is no longer greyed-out, and a HMR may now be opened by clicking this button.

If you want to review a case that you have already assessed, simply click the "Open button". Reviewing and modifying a completed case is described in Section 3.2.3.

3.2.2 Assessing a case

Once a case is made "Active" and the "Open" button is clicked, you will be taken to the **Case Review Screen** (Figure 3.3). This screen presents an overview of all of the information that was available to the pharmacist who performed the HMR.

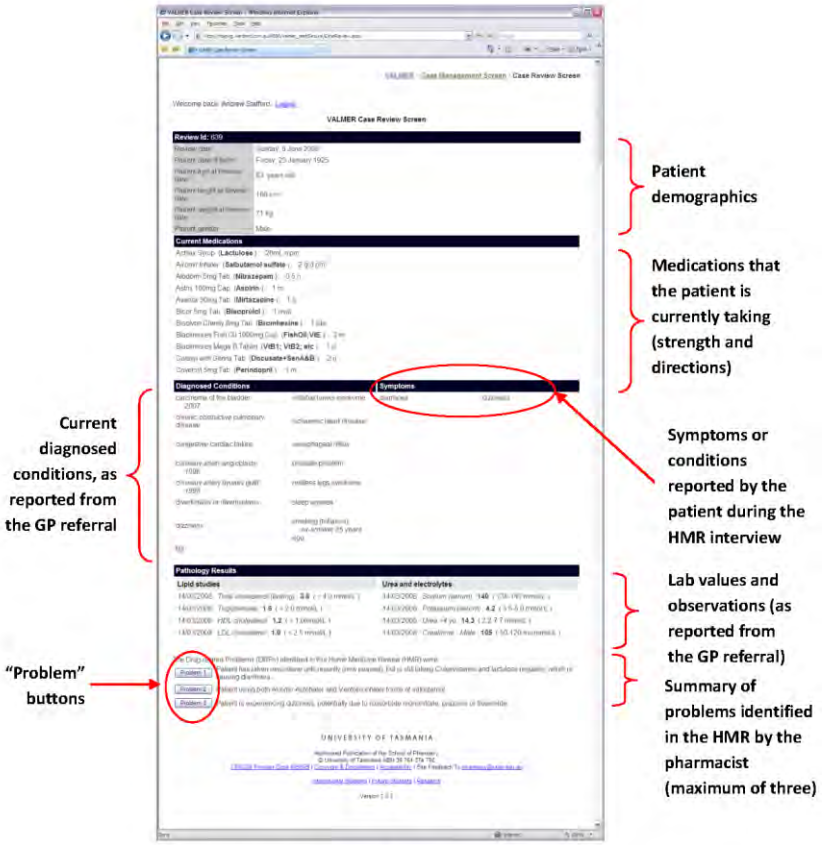


Figure 3.3 - Case Review Screen

The interventions which you are asked to assess are listed at the bottom of this screen (maximum of three). Clicking any of the "Problem" buttons at the bottom of the screen will take you to the **Case Assessment Screen** (Figure 3.4), where the assignment of consequences and their probabilities is performed.

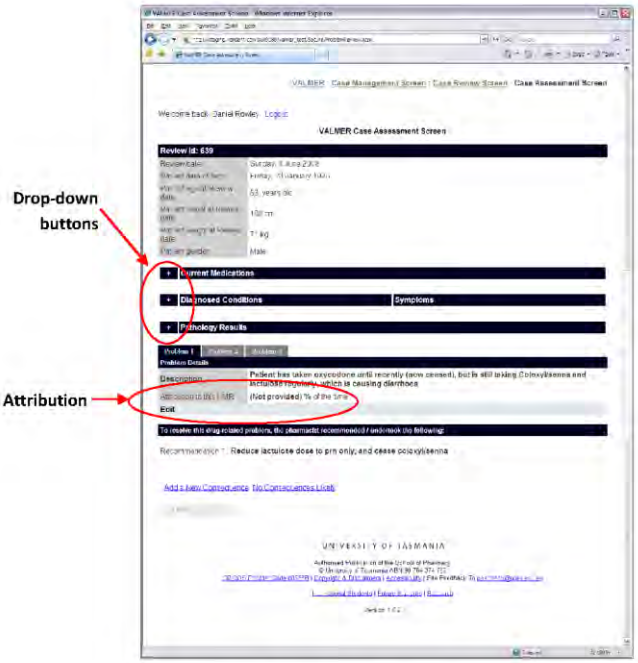


Figure 3.4 - Case Assessment Screen

The Case Assessment Screen contains all of the information that was presented to you on the previous screen, however much of it is hidden for simplicity (medications, conditions, symptoms and lab results). This information may be viewed at any time by clicking the drop-down icon beside each of these fields.

The first step in assessing each intervention is to assign an "Attribution" to it. This is an indication of the likelihood that only the pharmacist who performed this HMR would identify this problem or make this intervention. For many of the interventions, it is possible that another party (such as a GP, community pharmacist, allied health professional etc) may identify the same problem and resolve it. Enter your attribution estimate as a percentage by clicking the "Edit" link in the Attribution section.

Once an attribution as been entered, you can commence assigning consequences to each intervention. If you believe that the intervention will have no effect on the patient's health, select "No Consequences likely". If you believe that the intervention will have an effect on the patient's likelihood of experiencing one or more consequences, select "Add a New Consequence" to reveal

the Consequences drop-down box. When a particular consequence is selected, the vignette for each level of severity is shown when the cursor hovers over the words "Mild", Moderate" or "Severe". Please enter a likelihood for the consequence occurring before and after the intervention for each level of severity (**as a percentage**). If you believe the likelihood of the consequence occurring at a particular severity level either before or after the HMR to be nil, enter 0.

An example of entering a consequence is shown in Figure 3.5.

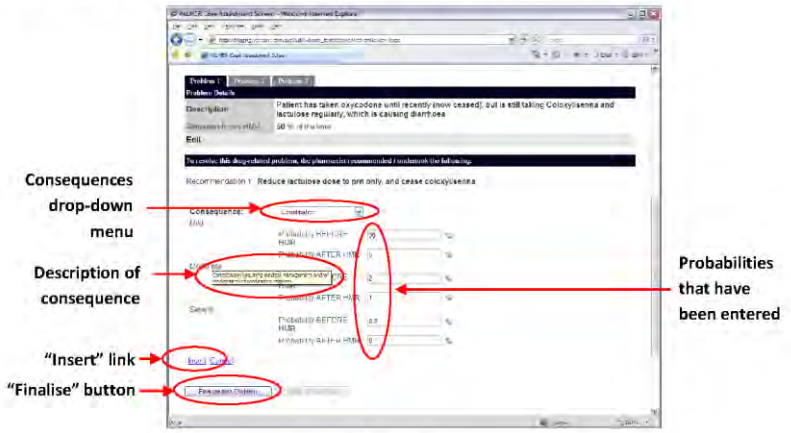


Figure 3.5 - Entry of Consequences

Once a value for each severity level, before and after the HMR, has been entered for the consequence, click "Insert". Once you have clicked "Insert", you may either add another consequence or, if you do not need to add any more consequences, "Finalise" the problem (intervention). Once a problem is "Finalised", you may then move on to assess the second and third interventions.

For a small number of cases, more than one recommendation is made per problem identified. In these cases, the assessment follows the same process as above, however each recommendation should be assessed independently from the other recommendations made to resolve that particular problem.

Once all of the interventions for a case have been assessed and "Finalised", the "Finalise this case" button will no longer be greyed out. Clicking this will return you to the "Case Management Screen", where you can either continue by assessing another HMR or log out of the system.

3.2.3 Insufficient information

Unfortunately, in some HMRs there may not be enough information provided to predict the potential outcome of an intervention. If this is the case, you can indicate that there is insufficient information to complete your assessment in the following way:

1. Reset the Attribution for the problem to "77%"
2. Click "No consequences likely"
3. Click "Finalise this problem"

Please use this function sparingly. Your assessments are intended to be an indication as to the likely outcomes of the interventions, and it is accepted that there will be significant limitations to this approach. Providing some indication as to the potential outcome of an intervention is valuable data, whereas providing no assessment is of limited value.

3.2.4 Editing a case

If you wish to edit your responses to a HMR that you have already finalised, this may be done from the Case Management Screen. Clicking the "Open" button beside the case which you want to open returns you to the Case Review Screen. Scroll down to the bottom of this screen and click any of the "Problem" buttons to open the Case Assessment Screen (Figure 3.6). Clicking the "Edit this Finalised Problem" button will unlock the case, allowing modification of the Attribution and consequences.

Once you are satisfied with your changes, click "Finalise this Problem" then "Finalise this Case".

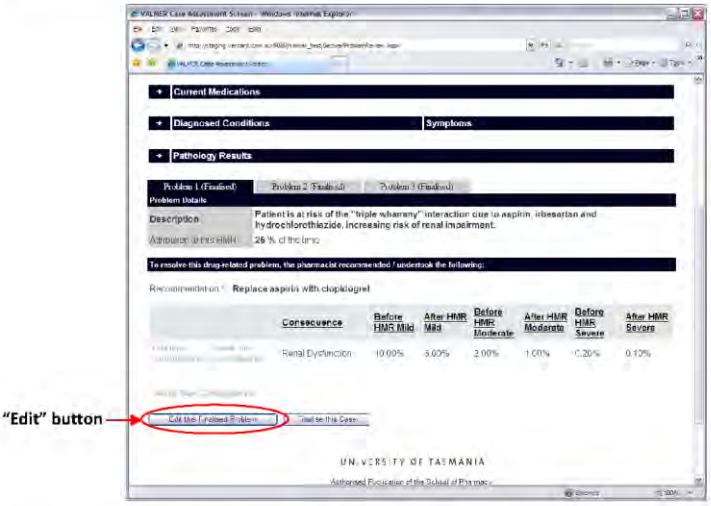


Figure 3.6 - Editing a Finalised Case

3.2.5 Unavailable consequence or other problems

It is possible that there will be situations where you feel that there is not an appropriate consequence for the intervention in the list of consequences provided. Unfortunately, adding consequences to the system is not possible at this point in time, but please contact Andrew Stafford at UTAS with details of the case to investigate options.

For any other issues with the system, please also contact Andrew Stafford.

3.3 Technical details

The VALMER website was programmed by the Verdant Group who also hosts the site.

The site has been designed and tested with the following browsers:

- Microsoft Internet Explorer version 7 and 8,
- Mozilla Firefox version 2 and 3, and
- Apple Safari version 3 (will also work with the iPhone).

Other browsers should be compatible but have not been tested.

4. Contact details

Project team:

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APPENDIX I – List of Consequences

Consequence	Severity level	Description
Acidosis	Mild	• Mild signs or symptoms of acidosis which resolve without intervention
	Moderate	• Moderate acidosis requiring medical management without hospitalisation
	Severe	• Severe acidosis requiring hospitalisation, electrolyte replacement and/or respiratory support
Alkalosis	Mild	• Mild signs or symptoms of alkalosis which resolve without intervention
	Moderate	• Moderate alkalosis requiring medical management without hospitalisation
	Severe	• Severe alkalosis requiring hospitalisation with electrolyte replacement
Allergic reaction	Mild	• Mild allergic reaction not requiring intervention
	Moderate	• Moderate allergic reaction requiring topical or oral medications
	Severe	• Severe allergic reaction requiring acute medical management
Anaemia	Mild	• Mild signs or symptoms of anaemia which resolve without intervention. E.g. haemoglobin of 100-109g/L in pregnant women, 110-119g/L in children and adult women, and 120-129g/L in adult men
	Moderate	• Anaemia requiring medical management and/or modification of medication regimen. E.g. haemoglobin of 70-99g/L in pregnant women, 80-109g/L in children and adult women, and 90-119g/L in adult men
	Severe	• Anaemia requiring hospitalisation and blood product or growth factor support. E.g. haemoglobin of 40-69g/L in pregnant women, 50-79g/L in children and adult women, and 60-89g/L in adult men.
Anxiety	Mild	• Mild signs or symptoms of anxiety which resolve without intervention
	Moderate	• Worsening of anxiety requiring modification of existing treatment regimen
	Severe	• Anxiety requiring specialist medical attention
Arrhythmia	Mild	• Arrhythmia that contributes to worsening of other cardiac conditions but not to such an extent as to require medical intervention
	Moderate	• Arrhythmia resulting in moderate haemodynamic or myocardial consequences requiring medical attention and treatment
	Severe	• Arrhythmia resulting in significant haemodynamic or myocardial complications requiring hospitalisation
Asthma	Mild	• Mild asthma which does not require additional intervention
	Moderate	• Moderate asthma requiring medical attention and/or modification of medications
	Severe	• Severe asthma requiring high level care in a hospital setting
Bleeding, non-specific	Mild	• Easy bruising, bleeding from small cuts, petechia, ecchymosis, mild elevation of INR not requiring adjustment of dosage
	Moderate	• Hematoma, epistaxis, blood loss from mouth, vagina, melena, eye bleed, haematuria, haematemesis, moderate elevation of INR requiring modification of dose of anticoagulant
	Severe	• Severe bleeding requiring hospitalisation, blood product and/or haemodynamic support.
Bone marrow suppression	Mild	• Mild signs or symptoms of bone marrow suppression which resolve without intervention
	Moderate	• Bone marrow suppression requiring medical management by modification of existing medication regimen
	Severe	• Bone marrow suppression requiring hospitalisation and blood product or growth factor support
Cerebrovascular event	Mild	• Mild symptoms which resolve (e.g. transient ischemic attack)
	Moderate	• Resulting in significant signs and symptoms requiring medical management (e.g. reversible ischaemic neurological deficit)

	Severe	• Resulting in severe symptoms and signs requiring hospitalisation and medical management (e.g stroke)
Chronic airways disease	**Mild**	• Mild chronic airways disease which does not require medical intervention
	Moderate	• Chronic airways disease requiring medical intervention and/or modification of medication
	Severe	• Severe chronic airways disease requiring hospitalisation and medical intervention
CNS depression	**Mild**	• CNS depression interfering with normal activities, but not requiring medical intervention
	Moderate	• CNS depression requiring medical attention and interfering significantly with normal activities
	Severe	• Significant CNS depression resulting in loss of consciousness or obtundation
Confusion	**Mild**	• Mild signs or symptoms of confusion which resolve without intervention
	Moderate	• Confusion requiring medical management and/or modification of medication regimen
	Severe	• Confusion requiring prompt medical management and investigation
Constipation	**Mild**	• Mild signs or symptoms of constipation likely to resolve without intervention
	Moderate	• Constipation requiring medical management and/or modification of medication regimen
	Severe	• Constipation requiring hospitalisation and medical and/or surgical management
Dementia	**Mild**	• Dementia resulting in some impairment of daily activities only
	Moderate	• Dementia to the extent that independent living is not possible without limited supervision
	Severe	• Dementia to the extent that permanent supervision is required
Depression	**Mild**	• Mild signs or symptoms of depression which resolve without intervention
	Moderate	• Worsening of depression requiring modification of treatment regimen
	Severe	• Destabilisation or unmasking of depression requiring specialist medical attention
Diabetes	**Mild**	• Reduced control of diabetes requiring increased monitoring
	Moderate	• Requiring modification of diabetes treatment regimen or significant complications requiring medical management
	Severe	• Complications of diabetes requiring specialist medical attention in hospital
Diarrhoea	**Mild**	• Mild signs or symptoms of diarrhoea likely to resolve without intervention
	Moderate	• Diarrhoea requiring medical management and/or modification of medication
	Severe	• Requiring hospitalisation for significant diarrhoea-related electrolyte and hydration complications
Gastrointestinal bleeding	**Mild**	• Occult gastrointestinal bleeding likely to require medical management only if persistent
	Moderate	• Overt gastrointestinal bleeding requiring medical management
	Severe	• Overt gastrointestinal bleeding with haemodynamic consequences requiring prompt medical management
Gastrointestinal pain	**Mild**	• Mild signs or symptoms of gastrointestinal pain likely to resolve without intervention
	Moderate	• Gastrointestinal pain requiring medical management and/or modification of medication regimen
	Severe	• Gastrointestinal pain requiring prompt medical management and investigation
Glaucoma	**Mild**	• Mild elevation of IOP not requiring intervention
	Moderate	• Moderate elevation of IOP requiring medical intervention
	Severe	• Severe glaucoma requiring acute medical or surgical intervention
Headache	**Mild**	• Mild signs or symptoms of headache which resolve without intervention
	Moderate	• Headache requiring oral analgesics and/or modification of medication regimen
	Severe	• Severe headache requiring acute medical management and hospitalisation
Heart failure	**Mild**	• Mild signs or symptoms of heart failure (e.g NYHA class II) which resolve without intervention

	Moderate	• Resulting in significant signs and symptoms of heart failure (e.g. NYHA class III) requiring medical management by modification of medication regimen
	Severe	• Significant signs and symptoms of heart failure (e.g. NYHA class IV) requiring hospitalisation and medical management (e.g. acute pulmonary oedema)
Hypercalcaemia	**Mild**	• Mild signs or symptoms of hypercalacemia which resolve without intervention
	Moderate	• Hypercalcaemia requiring medical management and/or modification of medication regimen
	Severe	• Hypercalcaemia requiring prompt medical management and investigation
Hyperkalaemia	**Mild**	• Mild signs or symptoms of hyperkalaemia which resolve without intervention
	Moderate	• Hyperkalaemia requiring medical management and/or modification of medication regimen
	Severe	• Hyperkalaemia requiring prompt medical management and investigation (e.g. palpitations, bradycardia)
Hypertension	**Mild**	• Mild signs or symptoms of hypertension which resolve without intervention
	Moderate	• Moderate elevation of blood pressure requiring modification of or commencement of medical management
	Severe	• Hypertension resulting in acute injury to target organs (e.g. renal, ocular or cerebral) requiring prompt medical management
Hyperthyroidism	**Mild**	• Mild signs or symptoms of hyperthyroidism likely to resolve without intervention
	Moderate	• Hyperthyroidism requiring medical management and/or modification of medication regimen
	Severe	• Signs or symptoms of hyperthyroidism requiring significant medical management and modification of medication regimen
Hypocalcaemia	**Mild**	• Mild signs or symptoms of hypocalcaemia which resolve without intervention
	Moderate	• Hypocalcaemia requiring medical management and/or modification of medication regimen
	Severe	• Hypocalcaemia requiring prompt medical management and investigation
Hypoglycaemia	**Mild**	• Mild signs or symptoms of hypoglycaemia which resolve without intervention
	Moderate	• Hypoglycaemia requiring additional oral medical management or modification of medication regimen
	Severe	• Hypoglycaemia requiring intravenous management
Hypokalaemia	**Mild**	• Mild signs or symptoms of hypokalaemia which resolve without intervention
	Moderate	• Hypokalaemia requiring medical management and/or modification of medication regimen
	Severe	• Hypokalaemia requiring prompt medical management and investigation (e.g. palpitations, tacchycardia)
Hypotension	**Mild**	• Clinical symptoms of hypotension not requiring medical intervention
	Moderate	• Hypotension requiring medical attention and modification of antihypertensive therapy.
	Severe	• Significant haemodynamic consequences of hypotension requiring hospitalisation and intravenous fluid support.
Hypothyroidism	**Mild**	• Mild signs or symptoms of hypothyroidism likely to resolve without intervention
	Moderate	• Hypothyroidism requiring medical management and/or modification of medication regimen
	Severe	• Signs or symptoms of hypothyroidism requiring significant medical management and modification of medication regimen
Infection, general	**Mild**	• Mild signs or symptoms of infection which resolve without intervention
	Moderate	• Infection with moderate complications requiring medical attention and oral antibiotics (e.g. PSI class I pneumonia)
	Severe	• Infection requiring hospitalisation and intravenous antibiotics (eg PSI class III pneumonia)
Insomnia	**Mild**	• Mild signs or symptoms of insomnia which resolve without intervention
	Moderate	• Insomnia requiring medical management
	Severe	• Insomnia requiring significant medical intervention and/or modification of medications
Liver disease	**Mild**	• Mild liver disease likely to resolve without intervention

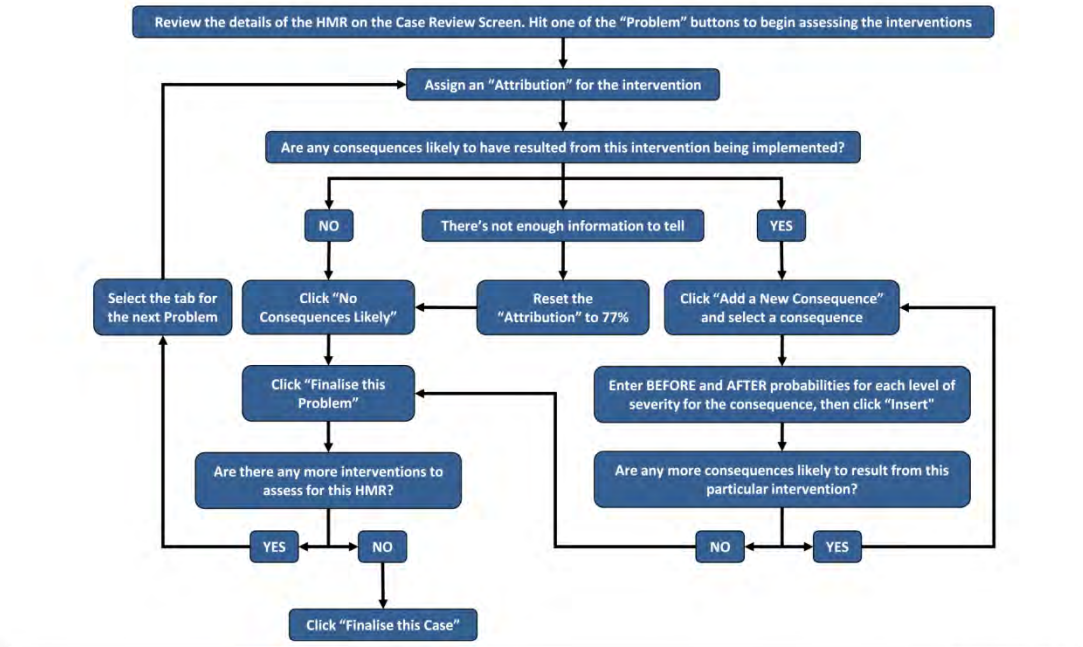
	Moderate	• Moderate liver disease requiring modification of medications and medical intervention
	Severe	• Severe liver disease requiring hospitalisation and acute medical management
Myocardial ischaemia	**Mild**	• Mild signs or symptoms of angina (e.g. NYHA class I to II) which resolve without intervention
	Moderate	• Moderate myocardial ischaemia resulting in significant signs and symptoms requiring medical management by modification of medication regimen (e.g. worsened stable angina)
	Severe	• Myocardial ischaemia resulting in severe symptoms and signs requiring hospitalisation and medical management (e.g unstable angina, myocardial infarction)
Myopathy	**Mild**	• Mild muscle pain not requiring intervention
	Mild	• Moderate muscle pain requiring modification of medications without elevation in creatine kinase
	Moderate	• Severe myopathy with elevation of creatine kinase requiring cessation of medication
Nausea	**Mild**	• Mild signs or symptoms of nausea likely to resolve without intervention
	Moderate	• Nausea requiring medical management and/or modification of medication
	Severe	• Requiring hospitalisation for significant vomiting-related electrolyte and hydration complications
Oedema	**Mild**	• Mild signs or symptoms of oedema which resolve without intervention
	Moderate	• Moderate oedema resulting in significant symptoms requiring medical management by modification of medication regimen
	Severe	• Significant oedema resulting in severe symptoms and signs requiring hospitalisation and management with intravenous diuretics
Osteoporosis	**Mild**	• Worsening of osteoporosis requiring increased monitoring
	Moderate	• Osteoporosis requiring modification of existing treatment regimen, or commencing treatment for an "at risk" person
	Severe	• Osteoporosis resulting in hospitalisation due to a major complication (e.g. fracture)
Pain	**Mild**	• Mild pain responding to currently prescribed agents
	Moderate	• Moderate pain requiring intensification of oral analgesics
	Severe	• Severe pain requiring management using specialist techniques or advice (e.g. hospitalisation, intravenous or epidural opioids or anaesthetics)
Parkinsonism	**Mild**	• Mild Parkinsonian symptoms of tremors and rigidity; slowness, impaired swallowing and speech; disturbance of equilibrium; patient is able to function indepedently
	Moderate	• Swallowing and speech severely impaired; autonomic nervous system disturbances; patients are ADL-dependent, but are able to move without help
	Severe	• Severe Parkinsonian symptoms- patient wheelchair and bed-bound; severely handicapped
Psychosis	**Mild**	• Mild signs or symptoms of psychosis which resolve without intervention
	Moderate	• Worsening of psychotic illness requiring modification of treatment regimen
	Severe	• Destabilisation or unmasking of psychosis requiring specialist medical attention
Rash	**Mild**	• Localised or mild rash symptoms which respond to "over the counter" treatment
	Moderate	• Rash requiring medical attention and topical and/or oral systemic reatment
	Severe	• Widespread rash with significant consequences requiring hospitalisation and intravenous systemic treatment
Renal dysfunction	**Mild**	• Mild signs or symptoms of renal dysfunction which resolve without intervention
	Moderate	• Renal dysfunction requiring medical management and/or modification of medication regimen
	Severe	• Acute decline in renal function requiring prompt medical management and investigation
Respiratory depression	**Mild**	• Mild respiratory depression which will resolve without medical intervention
	Moderate	• Requiring medical intervention and/or modification of medications

	Severe	• Severe respiratory depression requiring hospitalisation and medical intervention
Seizures	**Mild**	• Mild one-off seizure unlikely to recur or require management
	Moderate	• Seizure requiring medical attention or modification of medication regimen
	Severe	• Severe seizures requiring hospitalisation and intravenous anticonvulsants
Serotonin toxicity	**Mild**	• Mild signs or symptoms of serotonin toxicity which resolve without intervention
	Moderate	• Serotonin toxicity requiring medical management and/or modification of medication regimen
	Severe	• Serotonin toxicity requiring prompt medical management and investigation (e.g euphoria, tremor, severe anxiety, palpitations)
Urinary incontinence	**Mild**	• Mild signs or symptoms of urinary incontinence which resolve without intervention
	Moderate	• Urinary incontinence requiring medical management and/or modification of medication regimen
	Severe	• Urinary incontinence requiring hospitalisation and medical and/or surgical management
Urinary retention	**Mild**	• Symptomatic urinary retention not requiring medical management
	Moderate	• Symptomatic urinary retention requiring medical management
	Severe	• Symptomatic urinary retention requiring catheterisation
Urinary tract infection	**Mild**	• Mild signs or symptoms of UTI which resolve without intervention
	Moderate	• Moderate UTI requiring medical attention and oral antibiotics
	Severe	• UTI requiring hospitalisation and intravenous antibiotics, e.g. pyelonephritis

VALMER HMR Assessment System
User Guide

UMORE
Unit for Medication Outcomes Research and Education

APPENDIX II – Summary Cheat Sheet



Appendix XII - Tenni's consequences table

TABLE 145 - CONSEQUENCES TABLE DEVELOPED BY TENNI

MDC Code	MDC heading	Sub-group Code	Subgroup	Sub-Group Severity Code	Subgroup Severity Description	Health Status Impact	Duration of Health Status Impact	Duration of Admission	Cost of Admission	Number of GP Consults	Cost of GP Consults	Number of Specialist Consults	Cost of Specialist Consults	Investigation or Other Cost (if not included in DRG cost)	Total Direct Costs	Admission Cost and Duration*	Investigation or Other Cost Notes (Schedule Fee, CMBS as at 1 Nov 2004)
16	blood and blood forming organs and immunological disorders	16.04	Allergic reaction	16.04Mild	Mild reaction not requiring intervention	1	15	0.00	$0	1	$28				$28		
16	blood and blood forming organs and immunological disorders	16.04	Allergic reaction	16.04Moderate	Moderate allergic reaction requiring topical or oral medications	2	30	0.00	$0	2	$56				$56		
16	blood and blood forming organs and immunological disorders	16.04	Allergic reaction	16.04Severe	Severe allergic reaction requiring acute medical management	3	60	1.32	$1 238	2	$56				$1 294	Z61Z	
16	blood and blood forming organs and immunological disorders	16.01	Anaemia	16.01Mild	Mild signs or symptoms which resolve without intervention	1	90	0.00	$0	2	$56			$18	$74		Bloods
16	blood and blood forming organs and immunological disorders	16.01	Anaemia	16.01Moderate	Requiring medical management and/or modification of medication regimen	2	90	0.00	$0	3	$84			$18	$102		Bloods
16	blood and blood forming organs and immunological disorders	16.01	Anaemia	16.01Severe	Requiring hospitalisation and blood product or growth factor support	3	90	4.58	$3 144	3	$84	1	$128		$3 356	Q61A,B.,C	
19	mental diseases and disorders	19.02	Anxiety	19.02Mild	Mild signs or symptoms which resolve without intervention	1	30	0.00	$0	2	$56				$56		

MDC Code	MDC heading	Sub-group Code	Subgroup	Sub-Group Severity Code	Subgroup Severity Description	Health Status Impact	Duration of Health Status Impact	Duration of Admission	Cost of Admission	Number of GP Consults	Cost of GP Consults	Number of Specialist Consults	Cost of Specialist Consults	Investigation or Other Cost (if not included in DRG cost)	Total Direct Costs	Admission Cost and Duration*	Investigation or Other Cost Notes (Schedule Fee, CMBS as at 1 Nov 2004)
19	mental diseases and disorders	19.02	Anxiety	19.02Moderate	Worsening of disease requiring modification of existing treatment regimen	2	90	0.00	$0	4	$112				$112		
19	mental diseases and disorders	19.02	Anxiety	19.02Severe	Requiring specialist medical attention	3	180	4.03	$2 595	4	$112	2	$192		$2 899	U65Z	
5	circulatory system	05.07	Arrhythmia	05.07Mild	Contributing to worsening of other cardiac conditions but not to such an extent as to require medical intervention	1	360	0.00	$0	2	$56			$44	$100		ECG, Bloods
5	circulatory system	05.07	Arrhythmia	05.07Moderate	Resulting in moderate haemodynamic or myocardial consequences requiring medical attention and treatment	2	180	0.00	$0	8	$224			$44	$268		ECG, Bloods
5	circulatory system	05.07	Arrhythmia	05.07Severe	Resulting in significant haemodynamic or myocardial complications requiring hospitalisation	3	180	4.10	$3 641	4	$112	2	$192		$3 945	F70A,B;F71A,B	
4	respiratory system	04.01	Asthma	04.01Mild	Mild asthma which does not require additional intervention	1	360	0.00	$0	2	$56				$56		
4	respiratory system	04.01	Asthma	04.01Moderate	Moderate asthma requiring medical attention and/or modification of medications	2	360	0.00	$0	6	$168			$18	$186		Bloods
4	respiratory system	04.01	Asthma	04.01Severe	Severe asthma requiring high level care in a hospital setting	3	360	3.59	$2 532	8	$224				$2 756	E69A,B,C	
14	pregnancy, childbirth and puerperium	14.01	Birth Defect	14.01Mild	Minor birth defect that does not affect the newborn	1	30	0.00	$0	1	$28				$28		
14	pregnancy, childbirth and puerperium	14.01	Birth Defect	14.01Moderate	Birth defect not affecting course of pregnancy but resulting in damage to the newborn	2	60	0.00	$0	2	$56				$56		
14	pregnancy, childbirth and puerperium	14.01	Birth Defect	14.01Severe	Severe birth defect requiring termination of pregnancy	3	90	2.00	$2 466	4	$112				$2 578	040Z	

MDC Code	MDC heading	Sub-group Code	Subgroup	Sub-Group Severity Code	Subgroup Severity Description	Health Status Impact	Duration of Health Status Impact	Duration of Admission	Cost of Admission	Number of GP Consults	Cost of GP Consults	Number of Specialist Consults	Cost of Specialist Consults	Investigation or Other Cost (if not included in DRG cost)	Total Direct Costs	Admission Cost and Duration*	Investigation or Other Cost Notes (Schedule Fee, CMBS as at 1 Nov 2004)
16	blood and blood forming organs and immunological disorders	16.03	Bleeding, non-specific	16.03Mild	Mild elevation of INR not requiring adjustment of dosage	1	30	0.00	$0	1	$28				$28		
16	blood and blood forming organs and immunological disorders	16.03	Bleeding, non-specific	16.03Moderate	Moderate elevation of INR requiring modification of dose of anticoagulant	2	60	0.00	$0	2	$56			$18	$74		Bloods
16	blood and blood forming organs and immunological disorders	16.03	Bleeding, non-specific	16.03Severe	Severe bleeding requiring hospitalisation, blood product and/or haemodynamic support	3	90	3.12	$2 952	2	$56	1	$128		$3 136	Average	
16	blood and blood forming organs and immunological disorders	16.02	Bone marrow suppression	16.02Mild	Mild signs or symptoms which resolve without intervention	1	30	0.00	$0	2	$56			$18	$74		Bloods
16	blood and blood forming organs and immunological disorders	16.02	Bone marrow suppression	16.02Moderate	Requiring medical management by modification of existing medication regimen	2	60	0.00	$0	4	$112			$18	$130		Bloods
16	blood and blood forming organs and immunological disorders	16.02	Bone marrow suppression	16.02Severe	Requiring hospitalisation and blood product or growth factor support	3	90	8.30	$9 359	4	$112	2	$192		$9 663		
5	circulatory system	05.05	Cerebrovascular event	05.05Mild	Mild symptoms which resolve (e.g. transient ischemic attack)	1	30	0.00	$0	4	$112			$285	$397		Bloods, ?CAT
5	circulatory system	05.05	Cerebrovascular event	05.05Moderate	Resulting in significant signs and symptoms requiring medical management (e.g. reversible ischaemic neurological deficit)	2	180	6.31	$4 032	6	$168				$4 200	B69A,B,C	
5	circulatory system	05.05	Cerebrovascular event	05.05Severe	Resulting in severe symptoms and signs requiring hospitalisation and medical management (e.g stroke)	3	360	8.14	$6 257	8	$224				$6 481	B70A,B,C,D	

MDC Code	MDC heading	Sub-group Code	Subgroup	Sub-Group Severity Code	Subgroup Severity Description	Health Status Impact	Duration of Health Status Impact	Duration of Admission	Cost of Admission	Number of GP Consults	Cost of GP Consults	Number of Specialist Consults	Cost of Specialist Consults	Investigation or Other Cost (if not included in DRG cost)	Total Direct Costs	Admission Cost and Duration*	Investigation or Other Cost Notes (Schedule Fee, CMBS as at 1 Nov 2004)
4	respiratory system	04.02	Chronic Airways Disease	04.02Mild	Mild disease which does not require medical intervention	1	360	0.00	$0	1	$28				$28		
4	respiratory system	04.02	Chronic Airways Disease	04.02Moderate	Requiring medical intervention and/or modification of medication	2	360	0.00	$0	6	$168			$18	$186		Bloods
4	respiratory system	04.02	Chronic Airways Disease	04.02Severe	Severe disease requiring hospitalisation and medical intervention	3	360	6.66	$4 191	8	$224				$4 415	E65A,B	
1	nervous system	01.04	CNS Depression	01.04Mild	Interfering with normal activities, but not requiring medical intervention	1	360	0.00	$0	0	$0				$0		
1	nervous system	01.04	CNS Depression	01.04Moderate	Requiring medical attention and interfering significantly with normal activities	2	90	0.00	$0	2	$56			$35	$91		Bloods
1	nervous system	01.04	CNS Depression	01.04Severe	Significant CNS depression resulting in loss of consciousness or obtundation	3	30	3.12	$2 952	4	$112				$3 064	Average	
6	digestive system	06.02	Constipation	06.02Mild	Mild signs or symptoms likely to resolve without intervention	1	90	0.00	$0	0	$0				$0		
6	digestive system	06.02	Constipation	06.02Moderate	Requiring medical management and/or modification of medication regimen	2	30	0.00	$0	2	$56				$56		
6	digestive system	06.02	Constipation	06.02Severe	Requiring hospitalisation and medical and/or surgical management	3	60	4.49	$3 158	4	$112				$3 270	G65A,B	
13	female reproductive system	13.01	Contraceptive Failure	13.01Mild	Interference with contraceptive efficacy not requiring additional contraceptive precautions	1	5	0.00	$0	1	$28				$28		
13	female reproductive system	13.01	Contraceptive Failure	13.01Moderate	Interference with contraceptive efficacy that requires additional contraceptive methods be used	2	30	0.00	$0	1	$28				$28		
13	female reproductive system	13.01	Contraceptive Failure	13.01Severe	Total contraceptive failure resulting in undesired pregnancy	3	30	2.00	$2 466	2	$56				$2 522	040Z	
19	mental diseases and disorders	19.04	Depression	19.04Mild	Mild signs or symptoms which resolve without intervention	1	180	0.00	$0	4	$112				$112		

MDC Code	MDC heading	Sub-group Code	Subgroup	Sub-Group Severity Code	Subgroup Severity Description	Health Status Impact	Duration of Health Status Impact	Duration of Admission	Cost of Admission	Number of GP Consults	Cost of GP Consults	Number of Specialist Consults	Cost of Specialist Consults	Investigation or Other Cost (if not included in DRG cost)	Total Direct Costs	Admission Cost and Duration*	Investigation or Other Cost Notes (Schedule Fee, CMBS as at 1 Nov 2004)
19	mental diseases and disorders	19.04	Depression	19.04Moderate	Worsening of disease requiring modification of treatment regimen	2	180	0.00	$0	5	$140	1	$128		$268		
19	mental diseases and disorders	19.04	Depression	19.04Severe	Destabilisation or unmasking of depression requiring specialist medical attention	3	360	12.45	$7 192	6	$168	2	$192		$7 553	U63A,B; U64Z	Psych Assessment
10	endocrine, nutritional and metabolic	10.01	Diabetes	10.01Mild	Reduced control of disease requiring increased monitoring	1	360	0.00	$0	4	$112			$18	$130		Bloods
10	endocrine, nutritional and metabolic	10.01	Diabetes	10.01Moderate	Requiring modification of treatment regimen or significant complications requiring medical management	2	360	0.00	$0	6	$168			$18	$186		Bloods
10	endocrine, nutritional and metabolic	10.01	Diabetes	10.01Severe	Complications of diabetes requiring specialist medical attention in hospital	3	360	5.78	$4 063	6	$168	2			$4 231	K60A,B	
6	digestive system	06.05	Diarrhoea	06.05Mild	Mild signs or symptoms likely to resolve without intervention	1	7	0.00	$0	1	$28				$28		
6	digestive system	06.05	Diarrhoea	06.05Moderate	Requiring medical management and/or modification of medication	2	14	0.00	$0	2	$56				$56		
6	digestive system	06.05	Diarrhoea	06.05Severe	Requiring hospitalisation for significant vomiting-related electrolyte and hydration complications	3	30	3.12	$2 952	2	$56				$3 008	Average	
6	digestive system	06.01	Gastrointestinal bleeding	06.01Mild	Occult gastrointestinal bleeding likely to require medical management only if persistent	1	180	0.00	$0	1	$28			$1 748	$1 776		Bloods, endoscopy
6	digestive system	06.01	Gastrointestinal bleeding	06.01Moderate	Overt gastrointestinal bleeding requiring medical management	2	60	1.68	$1 199	1	$28	1	$128	$1 748	$3 103	G61B	Bloods, endoscopy
6	digestive system	06.01	Gastrointestinal bleeding	06.01Severe	Overt gastrointestinal bleeding with haemodynamic consequences requiring prompt medical management	3	90	3.58	$2 477	2	$56	2	$192		$2 725	G61A	
6	digestive system	06.03	Gastrointestinal pain	06.03Mild	Mild signs or symptoms likely to resolve without intervention	1	180	0.00	$0	2	$56			$18	$74		Bloods

MDC Code	MDC heading	Sub-group Code	Subgroup	Sub-Group Severity Code	Subgroup Severity Description	Health Status Impact	Duration of Health Status Impact	Duration of Admission	Cost of Admission	Number of GP Consults	Cost of GP Consults	Number of Specialist Consults	Cost of Specialist Consults	Investigation or Other Cost (if not included in DRG cost)	Total Direct Costs	Admission Cost and Duration*	Investigation or Other Cost Notes (Schedule Fee, CMBS as at 1 Nov 2004)
6	digestive system	06.03	Gastrointestinal pain	06.03Moderate	Requiring medical management and/or modification of medication regimen	2	180	0.00	$0	5	$140	1	$128	$1 748	$2 016		Endoscopy, Bloods
6	digestive system	06.03	Gastrointestinal pain	06.03Severe	Requiring prompt medical management and investigation	3	60	5.44	$3 628	1	$28	1	$128		$3 784	G67A	
2	eye	02.01	Glaucoma	02.01Mild	Mild elevation of IOP not requiring intervention	1	360	0.00	$0	0	$0				$0		
2	eye	02.01	Glaucoma	02.01Moderate	Moderate elevation of IOP requiring medical intervention	2	180	0.00	$0	1	$28	2		$192	$220		
2	eye	02.01	Glaucoma	02.01Severe	Severe glaucoma requiring acute medical or surgical intervention	3	90	3.12	$2 952	1	$28	3		$256	$3 236	Average	
1	nervous system	01.02	Headache	01.02Mild	Mild signs or symptoms which resolve without intervention	1	7	0.00	$0	0	$0				$0		
1	nervous system	01.02	Headache	01.02Moderate	Headache requiring oral analgesics and/or modification of medication regimen	2	30	0.00	$0	2	$56			$268	$324		Bloods, CT
1	nervous system	01.02	Headache	01.02Severe	Severe headache requiring acute medical management and hospitalisation	3	90	1.73	$1 280	4	$112				$1 392	B77Z Headache	
5	circulatory system	05.06	Heart Failure	05.06Mild	Mild signs or symptoms which resolve without intervention	1	60	0.00	$0	2	$56			$35	$91		Bloods
5	circulatory system	05.06	Heart Failure	05.06Moderate	Resulting in significant signs and symptoms requiring medical management by modification of medication regimen	2	360	0.00	$0	8	$224			$35	$259		Bloods
5	circulatory system	05.06	Heart Failure	05.06Severe	Significant signs and symptoms requiring hospitalisation and medical management (e.g. acute pulmonary oedema)	3	360	7.58	$5 368	4	$112	2	$192	$35	$5 707	E64Z, F62A,B	
10	endocrine, nutritional and metabolic	10.03	Hypercalcaemia	10.03Mild	Mild signs or symptoms which resolve without intervention	1	30	0.00	$0	1	$28				$28		
10	endocrine, nutritional and metabolic	10.03	Hypercalcaemia	10.03Moderate	Requiring medical management and/or modification of medication regimen	2	60	0.00	$0	2	$56			$18	$74		Bloods

MDC Code	MDC heading	Sub-group Code	Subgroup	Sub-Group Severity Code	Subgroup Severity Description	Health Status Impact	Duration of Health Status Impact	Duration of Admission	Cost of Admission	Number of GP Consults	Cost of GP Consults	Number of Specialist Consults	Cost of Specialist Consults	Investigation or Other Cost (if not included in DRG cost)	Total Direct Costs	Admission Cost and Duration*	Investigation or Other Cost Notes (Schedule Fee, CMBS as at 1 Nov 2004)
10	endocrine, nutritional and metabolic	10.03	Hypercalcaemia	10.03Severe	Requiring prompt medical management and investigation	3	90	3.12	$2 952	3	$84				$3 036	Average	
10	endocrine, nutritional and metabolic	10.05	Hyperkalaemia	10.05Mild	Mild signs or symptoms which resolve without intervention	1	30	0.00	$0	1	$28				$28		
10	endocrine, nutritional and metabolic	10.05	Hyperkalaemia	10.05Moderate	Requiring medical management and/or modification of medication regimen	2	60	0.00	$0	2	$56			$18	$74		Bloods
10	endocrine, nutritional and metabolic	10.05	Hyperkalaemia	10.05Severe	Requiring prompt medical management and investigation (e.g. palpitations, bradycardia)	3	90	3.12	$2 952	3	$84				$3 036	Average	
5	circulatory system	05.02	Hypertension	05.02Mild	Mild signs or symptoms which resolve without intervention	1	360	0.00	$0	1	$28				$28		
5	circulatory system	05.02	Hypertension	05.02Moderate	Moderate elevation of blood pressure requiring modification of or commencement of medical management	2	360	0.00	$0	8	$224			$18	$242		Bloods, Lipids
5	circulatory system	05.02	Hypertension	05.02Severe	Acute injury to target organs (e.g. renal, ocular or cerebral) requiring prompt medical management	3	90	3.65	$2 381	6	$168				$2 549	F67A,B	
10	endocrine, nutritional and metabolic	10.04	Hypocalcaemia	10.04Mild	Mild signs or symptoms which resolve without intervention	1	30	0.00	$0	1	$28				$28		
10	endocrine, nutritional and metabolic	10.04	Hypocalcaemia	10.04Moderate	Requiring medical management and/or modification of medication regimen	2	60	0.00	$0	2	$56			$18	$74		Bloods
10	endocrine, nutritional and metabolic	10.04	Hypocalcaemia	10.04Severe	Requiring prompt medical management and investigation	3	90	3.12	$2 952	3	$84				$3 036	Average	
10	endocrine, nutritional and metabolic	10.07	Hypoglycaemia	10.07Mild	Mild signs or symptoms which resolve without intervention	1	30	0.00	$0	1	$28				$28		

MDC Code	MDC heading	Sub-group Code	Subgroup	Sub-Group Severity Code	Subgroup Severity Description	Health Status Impact	Duration of Health Status Impact	Duration of Admission	Cost of Admission	Number of GP Consults	Cost of GP Consults	Number of Specialist Consults	Cost of Specialist Consults	Investigation or Other Cost (if not included in DRG cost)	Total Direct Costs	Admission Cost and Duration*	Investigation or Other Cost Notes (Schedule Fee, CMBS as at 1 Nov 2004)
10	endocrine, nutritional and metabolic	10.07	Hypoglycaemia	10.07Moderate	Requiring additional oral medical management or modification of medication regimen	2	60	0.00	$0	2	$56			$18	$74		Bloods
10	endocrine, nutritional and metabolic	10.07	Hypoglycaemia	10.07Severe	Requiring intravenous management	3	90	3.12	$2 952	3	$84				$3 036	Average	
10	endocrine, nutritional and metabolic	10.08	Hypokalaemia	10.08Mild	Mild signs or symptoms which resolve without intervention	1	30	0.00	$0	1	$28				$28		
10	endocrine, nutritional and metabolic	10.08	Hypokalaemia	10.08Moderate	Requiring medical management and/or modification of medication regimen	2	60	0.00	$0	2	$56			$18	$74		Bloods
10	endocrine, nutritional and metabolic	10.08	Hypokalaemia	10.08Severe	Requiring prompt medical management and investigation (e.g. palpitations, tacchycardia)	3	90	3.12	$2 952	3	$84				$3 036	Average	
5	circulatory system	05.01	Hypotension	05.01Mild	Clinical symptoms of hypotension not requiring medical intervention	1	90	0.00	$0	1	$28				$28		
5	circulatory system	05.01	Hypotension	05.01Moderate	Requiring medical attention and modification of antihypertensive therapy.	2	60	0.00	$0	4	$112				$112		
5	circulatory system	05.01	Hypotension	05.01Severe	Significant haemodynamic consequences requiring hospitalisation and intravenous fluid support.	3	30	3.12	$2 952	6	$168				$3 120	Average	
10	endocrine, nutritional and metabolic	10.06	Hypothyroidism	10.06Mild	Requiring medical management by modification of medication regimen	1	30	0.00	$0	1	$28				$28		
10	endocrine, nutritional and metabolic	10.06	Hypothyroidism	10.06Moderate	Requiring medical management and/or modification of medication regimen	2	60	0.00	$0	2	$56			$18	$74		Bloods
10	endocrine, nutritional and metabolic	10.06	Hypothyroidism	10.06Severe	Mild signs or symptoms likely to resolve without intervention	3	90	3.12	$2 952	3	$84				$3 036	Average	

MDC Code	MDC heading	Sub-group Code	Subgroup	Sub-Group Severity Code	Subgroup Severity Description	Health Status Impact	Duration of Health Status Impact	Duration of Admission	Cost of Admission	Number of GP Consults	Cost of GP Consults	Number of Specialist Consults	Cost of Specialist Consults	Investigation or Other Cost (if not included in DRG cost)	Total Direct Costs	Admission Cost and Duration*	Investigation or Other Cost Notes (Schedule Fee, CMBS as at 1 Nov 2004)
18	infectious and parasitic diseases	18.01	Infection, general	18.01Mild	Mild signs or symptoms which resolve without intervention	1	15	0.00	$0	1	$28				$28		
18	infectious and parasitic diseases	18.01	Infection, general	18.01Moderate	Moderate complications requiring medical attention and oral antibiotics	2	30	0.00	$0	2	$56			$34	$90		MCS
18	infectious and parasitic diseases	18.01	Infection, general	18.01Severe	Requiring hospitalisation and intravenous antibiotics	3	30	7.84	$5 946	2	$56				$6 002	E62A,B,C;T60A,B	
7	hepatobiliary system and pancreas	07.01	Liver Disease	07.01Mild	Mild liver disease likely to resolve without intervention	1	30	0.00	$0	2	$56				$56		
7	hepatobiliary system and pancreas	07.01	Liver Disease	07.01Moderate	Moderate liver disease requiring modification of medications and medical intervention	2	60	0.00	$0	7	$196	1	$128	$18	$342		Bloods
7	hepatobiliary system and pancreas	07.01	Liver Disease	07.01Severe	Severe liver disease requiring hospitalisation and acute medical management	3	90	6.70	$4 936	3	$84	1	$128		$5 148	H60A,B.C	
5	circulatory system	05.04	Myocardial Ischaemia	05.04Mild	Mild signs or symptoms which resolve without intervention	1	360	0.00	$0	2	$56			$35	$91		Bloods
5	circulatory system	05.04	Myocardial Ischaemia	05.04Moderate	Moderate ischaemia resulting in significant signs and symptoms requiring medical management by modification of medication regimen (e.g. worsened stable angina)	2	360	1.60	$1 278	2	$56	2	$192		$1 526	F74Z	
5	circulatory system	05.04	Myocardial Ischaemia	05.04Severe	Resulting in severe symptoms and signs requiring hospitalisation and medical management (e.g unstable angina, myocardial infarction)	3	360	4.75	$4 526	4	$112	2			$4 639	F41, A,B, F42A,B,F60A,B,C; F72A,B	
8	musculoskeletal system and connective tissue	08.01	Myopathy	08.01Mild	Mild muscle pain not requiring intervention	1	90	0.00	$0	2	$56				$56		
8	musculoskeletal system and connective tissue	08.01	Myopathy	08.01Moderate	Moderate muscle pain requiring modification of medications without elevation in creatine kinase	1	60	0.00	$0	4	$112			$59	$171		Bloods, CK

MDC Code	MDC heading	Sub-group Code	Subgroup	Sub-Group Severity Code	Subgroup Severity Description	Health Status Impact	Duration of Health Status Impact	Duration of Admission	Cost of Admission	Number of GP Consults	Cost of GP Consults	Number of Specialist Consults	Cost of Specialist Consults	Investigation or Other Cost (if not included in DRG cost)	Total Direct Costs	Admission Cost and Duration*	Investigation or Other Cost Notes (Schedule Fee, CMBS as at 1 Nov 2004)
8	musculoskeletal system and connective tissue	08.01	Myopathy	08.01Severe	Severe myopathy with elevation of creatine kinase requiring cessation of medication	2	30	0.00	$0	6	$168			$59	$227		Bloods, CK
6	digestive system	06.04	Nausea	06.04Mild	Mild signs or symptoms likely to resolve without intervention	1	7	0.00	$0	1	$28				$28		
6	digestive system	06.04	Nausea	06.04Moderate	Requiring medical management and/or modification of medication	2	14	0.00	$0	2	$56				$56		
6	digestive system	06.04	Nausea	06.04Severe	Requiring hospitalisation for significant vomiting-related electrolyte and hydration complications	3	30	3.12	$2 952	2	$56				$3 008	Average	
5	circulatory system	05.03	Oedema	05.03Mild	Mild signs or symptoms which resolve without intervention	1	90	0.00	$0	1	$28				$28		
5	circulatory system	05.03	Oedema	05.03Moderate	Moderate oedema resulting in significant symptoms requiring medical management by modification of medication regimen	2	90	0.00	$0	6	$168			$18	$186		Bloods
5	circulatory system	05.03	Oedema	05.03Severe	Significant oedema resulting in severe symptoms and signs requiring hospitalisation and management with intravenous diuretics	3	30	6.16	$4 992	4	$112				$5 104	E64Z,	
18	infectious and parasitic diseases	18.04	Ophthalmic Herpes	18.04Mild	Mild signs or symptoms likely to resolve without medical intervention	1	30	0.00	$0	2	$56				$56		
18	infectious and parasitic diseases	18.04	Ophthalmic Herpes	18.04Moderate	Requiring medical management and/or modification of medications	2	30	0.00	$0	2	$56				$56		
18	infectious and parasitic diseases	18.04	Ophthalmic Herpes	18.04Severe	Severe ocular infection requiring hospitalisation and intravenous management	3	30	5.91	$3 864	0	$0	2	$192		$4 056	C60A,B	
10	endocrine, nutritional and metabolic	10.02	Osteoporosis	10.02Mild	Worsening of disease requiring increased monitoring	1	360	0.00	$0	4	$112			$83	$195		Bone Densitometry item 12306-12301, Bloods

MDC Code	MDC heading	Sub-group Code	Subgroup	Sub-Group Severity Code	Subgroup Severity Description	Health Status Impact	Duration of Health Status Impact	Duration of Admission	Cost of Admission	Number of GP Consults	Cost of GP Consults	Number of Specialist Consults	Cost of Specialist Consults	Investigation or Other Cost (if not included in DRG cost)	Total Direct Costs	Admission Cost and Duration*	Investigation or Other Cost Notes (Schedule Fee, CMBS as at 1 Nov 2004)
10	endocrine, nutritional and metabolic	10.02	Osteoporosis	10.02Moderate	Requiring modification of existing treatment regimen (e.g commencing treatment for an "at risk" person)	2	60	0.00	$0	6	$168			$83	$251		Bone Densitometry item 12306-12301, Bloods
10	endocrine, nutritional and metabolic	10.02	Osteoporosis	10.02Severe	Resulting in hospitalisation due to a major complication (e.g. fracture)	3	90	10.76	$7 317	8	$224				$7 541	I60Z;I61Z;I62A,B	
18	infectious and parasitic diseases	18.03	Otitis Media	18.03Mild	Mild signs and symptoms that will resolve without medical intervention	1	15	0.00	$0	1	$28				$28		
18	infectious and parasitic diseases	18.03	Otitis Media	18.03Moderate	Requiring medical intervention and/or modification of medications	2	30	0.00	$0	2	$56				$56		
18	infectious and parasitic diseases	18.03	Otitis Media	18.03Severe	Severe otitis media requiring hospitalisation and intravenous antibiotic management	3	30	2.32	$1 932	2	$56				$1 988	D63A,B	
1	nervous system	01.03	Pain	01.03Mild	Mild pain responding to currently prescribed agents	1	7	0.00	$0	2	$56				$56		
1	nervous system	01.03	Pain	01.03Moderate	Moderate pain requiring intensification of oral analgesics	2	30	0.00	$0	4	$112				$112		
1	nervous system	01.03	Pain	01.03Severe	Severe pain requiring management using specialist techniques or advice (e.g. hospitalisation, intravenous or epidural opioids or anaesthetics)	3	90	3.12	$2 952	4	$112	2	$192		$3 256	Average	
19	mental diseases and disorders	19.01	Psychosis	19.01Mild	Mild signs or symptoms which resolve without intervention	1	180	0.00	$0	1	$28				$28		
19	mental diseases and disorders	19.01	Psychosis	19.01Moderate	Worsening of disease requiring modification of treatment regimen	2	180	0.00	$0	2	$56				$56		
19	mental diseases and disorders	19.01	Psychosis	19.01Severe	Destabilisation or unmasking of psychosis requiring specialist medical attention	3	360	10.89	$7 491	0	$0	4	$320		$7 811	U62A,B	
9	skin, subcutaneous tissue and breast	09.01	Rash	09.01Mild	Localised or mild symptoms which respond to "over the counter" treatment	1	15	0.00	$0	1	$28				$28		

MDC Code	MDC heading	Sub-group Code	Subgroup	Sub-Group Severity Code	Subgroup Severity Description	Health Status Impact	Duration of Health Status Impact	Duration of Admission	Cost of Admission	Number of GP Consults	Cost of GP Consults	Number of Specialist Consults	Cost of Specialist Consults	Investigation or Other Cost (if not included in DRG cost)	Total Direct Costs	Admission Cost and Duration*	Investigation or Other Cost Notes (Schedule Fee, CMBS as at 1 Nov 2004)
9	skin, subcutaneous tissue and breast	09.01	Rash	09.01Moderate	Requiring medical attention and topical and/or oral systemic reatment	2	60	0.00	$0	2	$56				$56		
9	skin, subcutaneous tissue and breast	09.01	Rash	09.01Severe	Widespread rash with significant consequences requiring hospitalisation and intravenous systemic treatment	3	180	3.44	$2 166	4	$112				$2 278	J61Z	
11	kidney and urinary	11.03	Renal Dysfunction	11.03Mild	Mild signs or symptoms which resolve without intervention	1	90	0.00	$0	2	$56				$56		
11	kidney and urinary	11.03	Renal Dysfunction	11.03Moderate	Requiring medical management and/or modification of medication regimen	2	180	0.00	$0	5	$140	1	$128	$18	$286		Bloods
11	kidney and urinary	11.03	Renal Dysfunction	11.03Severe	Acute decline in renal function requiring prompt medical management and investigation	3	360	7.26	$5 614	6	$168	2	$192		$5 974	L60A,B,C	
4	respiratory system	04.03	Respiratory depression	04.03Mild	Mild respiratory depression which will resolve without medical intervention	1	7	0.00	$0	1	$28				$28		
4	respiratory system	04.03	Respiratory depression	04.03Moderate	Requiring medical intervention and/or modification of medications	2	14	0.00	$0	2	$56			$18	$74		Bloods
4	respiratory system	04.03	Respiratory depression	04.03Severe	Severe respiratory depression requiring hospitalisation and medical intervention	3	30	3.12	$2 952	2	$56				$3 008	Average	
1	nervous system	01.01	Seizures	01.01Mild	Mild one-off seizure unlikely to recur or require management	1	7	0.00	$0	2	$56			$104	$160		EEG
1	nervous system	01.01	Seizures	01.01Moderate	Requiring medical attention or modification of medication regimen	2	60	0.00	$0	4	$112			$122	$234		EEG, Bloods
1	nervous system	01.01	Seizures	01.01Severe	Severe seizures requiring hospitalisation and intravenous anticonvulsants	3	90	2.05	$1 606	2	$56	2	$192		$1 854	B76B Seizure	
19	mental diseases and disorders	19.03	Serotonin Syndrome	19.03Mild	Mild signs or symptoms which resolve without intervention	1	14	0.00	$0	1	$28				$28		
19	mental diseases and disorders	19.03	Serotonin Syndrome	19.03Moderate	Requiring medical management and/or modification of medication regimen	2	30	0.00	$0	2	$56				$56		

MDC Code	MDC heading	Sub-group Code	Subgroup	Sub-Group Severity Code	Subgroup Severity Description	Health Status Impact	Duration of Health Status Impact	Duration of Admission	Cost of Admission	Number of GP Consults	Cost of GP Consults	Number of Specialist Consults	Cost of Specialist Consults	Investigation or Other Cost (if not included in DRG cost)	Total Direct Costs	Admission Cost and Duration*	Investigation or Other Cost Notes (Schedule Fee, CMBS as at 1 Nov 2004)
19	mental diseases and disorders	19.03	Serotonin Syndrome	19.03Severe	Requiring prompt medical management and investigation (e.g euphoria, tremor, severe anxiety, palpitations)	3	30	0.00	$0	2	$56			$18	$74		Bloods
11	kidney and urinary	11.02	Urinary Incontinence	11.02Mild	Mild signs or symptoms which resolve without intervention	1	30	0.00	$0	1	$28				$28		
11	kidney and urinary	11.02	Urinary Incontinence	11.02Moderate	Requiring medical management and/or modification of medication regimen	2	60	0.00	$0	2	$56				$56		
11	kidney and urinary	11.02	Urinary Incontinence	11.02Severe	Requiring hospitalisation and medical and/or surgical management	3	90	3.12	$2 952	3	$84				$3 036	Average	
11	kidney and urinary	11.01	Urinary retention	11.01Mild	Symptomatic, but not requiring medical management	1	30	0.00	$0	1	$28				$28		
11	kidney and urinary	11.01	Urinary retention	11.01Moderate	Requiring medical management	2	60	0.00	$0	2	$56			$18	$74		?IVP, Bloods
11	kidney and urinary	11.01	Urinary retention	11.01Severe	Requiring catheterisation	3	90	2.66	$2 949	4	$112				$3 061	L08A,B	
18	infectious and parasitic diseases	18.02	Urinary Tract Infection	18.02Mild	Mild signs or symptoms which resolve without intervention	1	15	0.00	$0	1	$28				$28		
18	infectious and parasitic diseases	18.02	Urinary Tract Infection	18.02Moderate	Moderate complications requiring medical attention and oral antibiotics	2	30	0.00	$0	2	$56			$34	$90		MCS
18	infectious and parasitic diseases	18.02	Urinary Tract Infection	18.02Severe	Requiring hospitalisation and intravenous antibiotics	3	30	6.26	$3 920	2	$56				$3 976	L63A,B,C	

* Source (National Hospital Cost Weights for AR-DRG Version 4.2, 2002-3)

Appendix XIII Advertisement to recruit GPs for consequences study

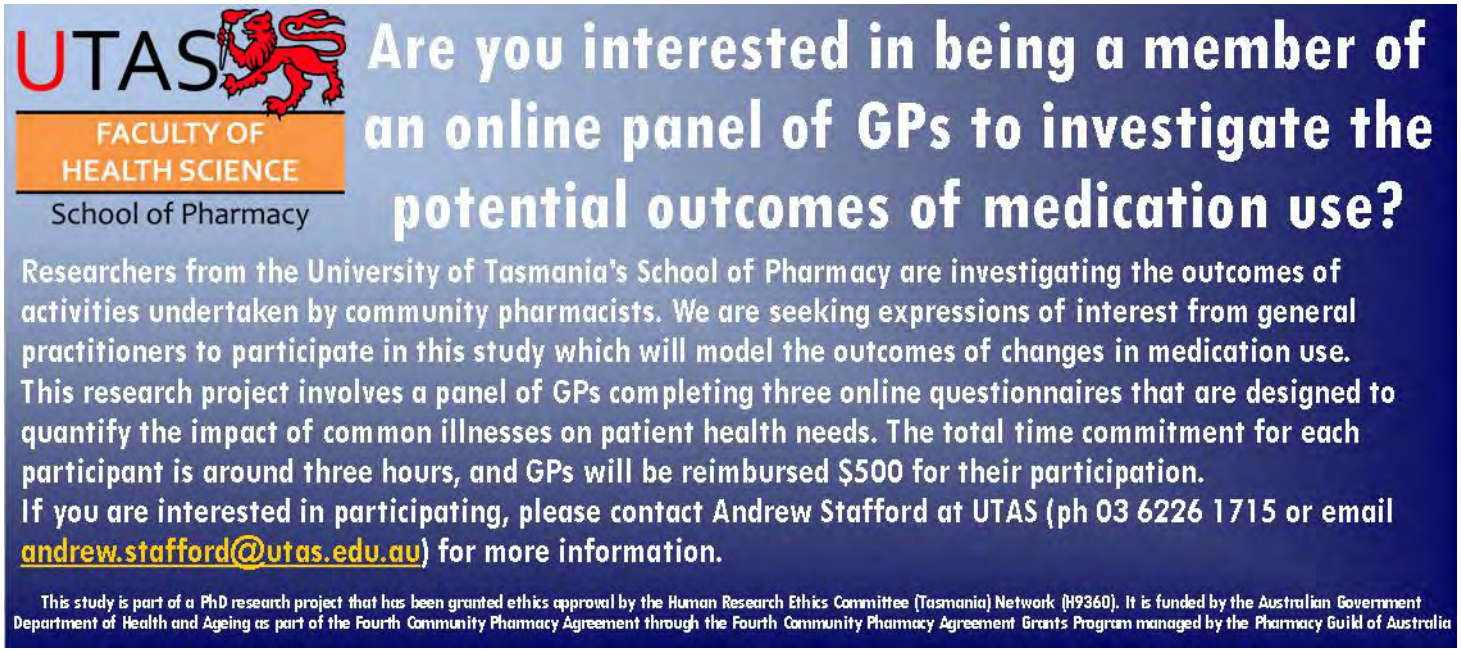
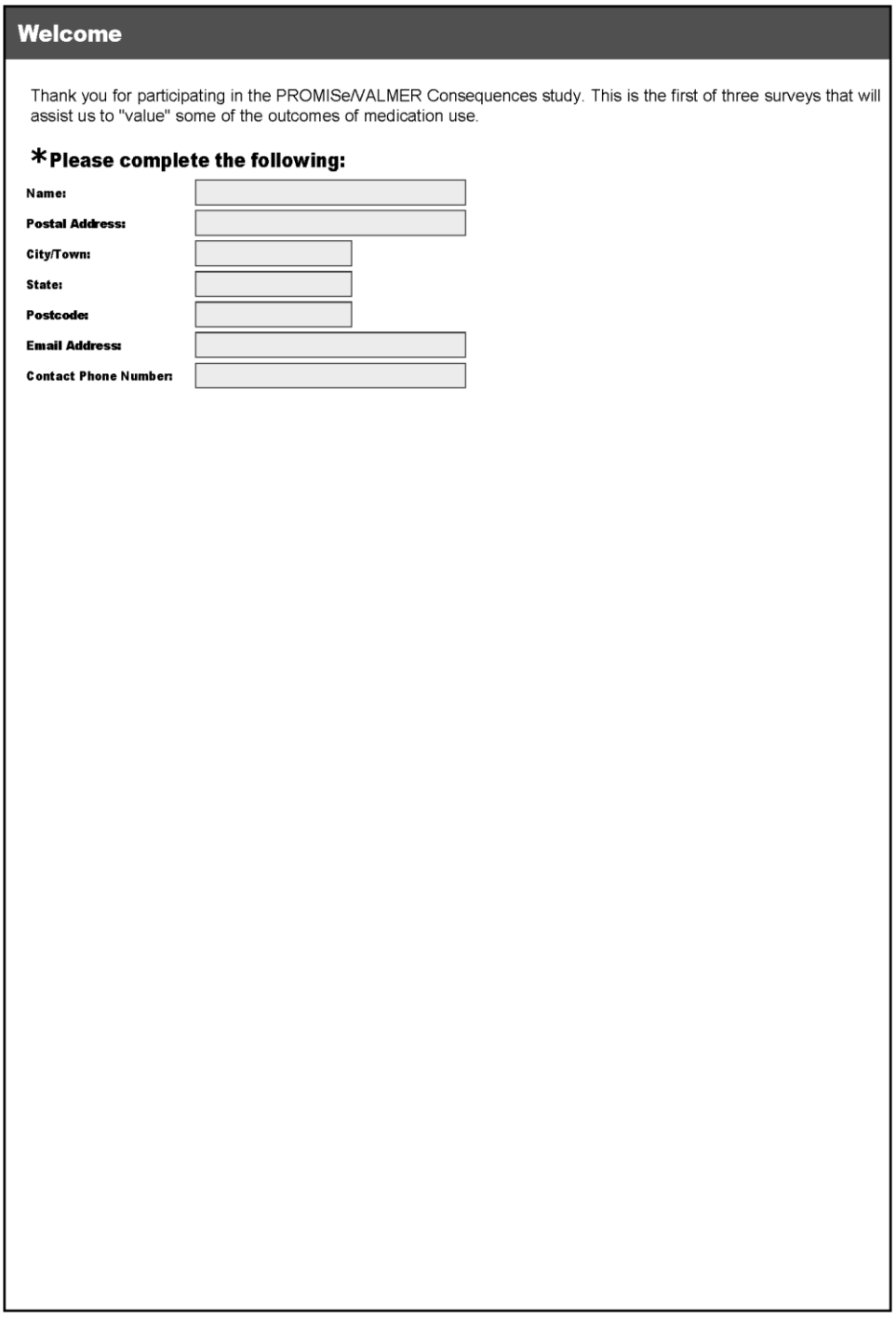


FIGURE 64 - ADVERTISEMENT TO RECRUIT GPS FOR CONSEQUENCES STUDY (IN 6MINUTES NEWSLETTER, AVAILABLE FROM 6MINUTES.COM.AU)

Appendix XIV - Questionnaire for GPs who participated in consequences study



Welcome

Thank you for participating in the PROMISe/VALMER Consequences study. This is the first of three surveys that will assist us to "value" some of the outcomes of medication use.

***Please complete the following:**

Name:

Postal Address:

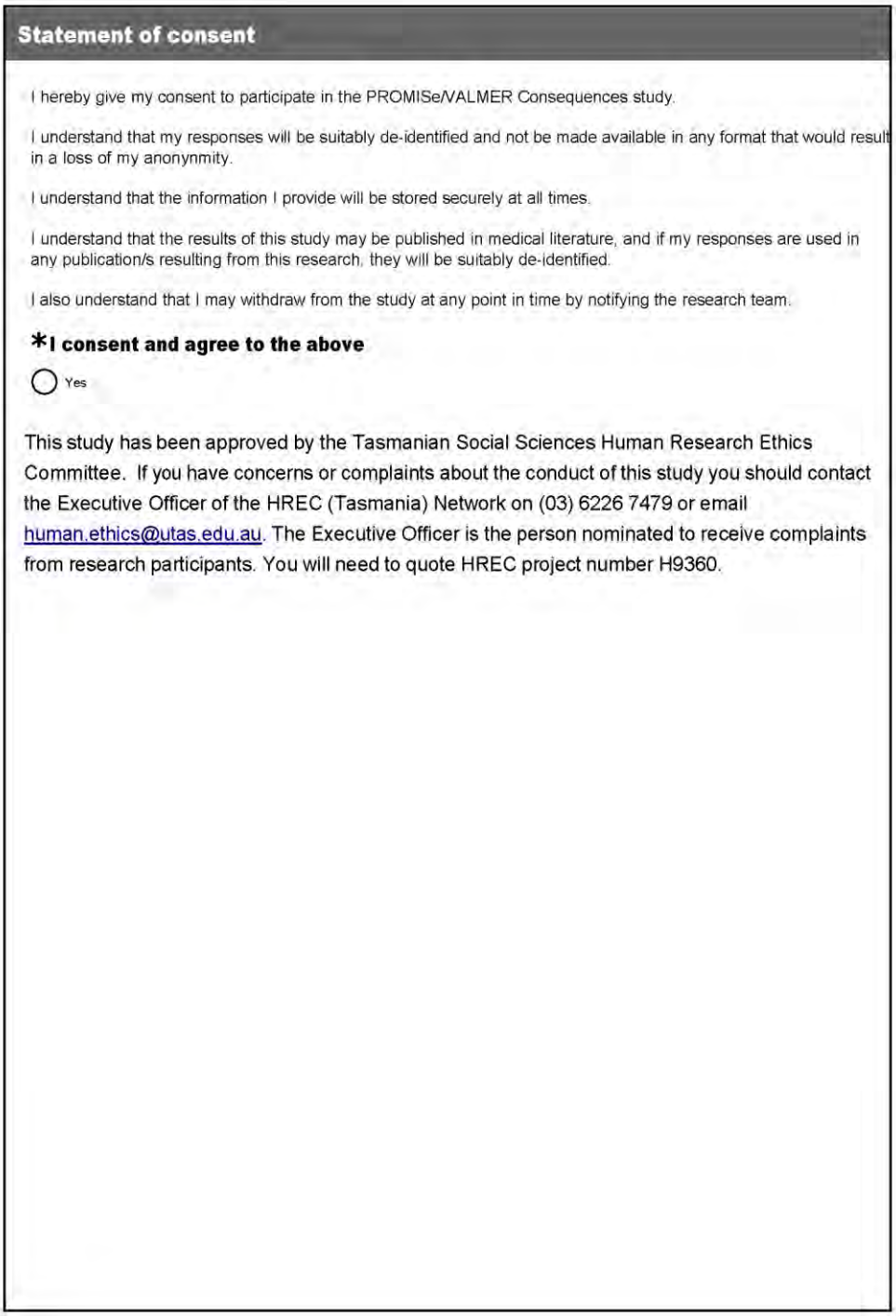
City/Town:

State:

Postcode:

Email Address:

Contact Phone Number:



Statement of consent

I hereby give my consent to participate in the PROMISe/VALMER Consequences study.

I understand that my responses will be suitably de-identified and not be made available in any format that would result in a loss of my anonymity.

I understand that the information I provide will be stored securely at all times.

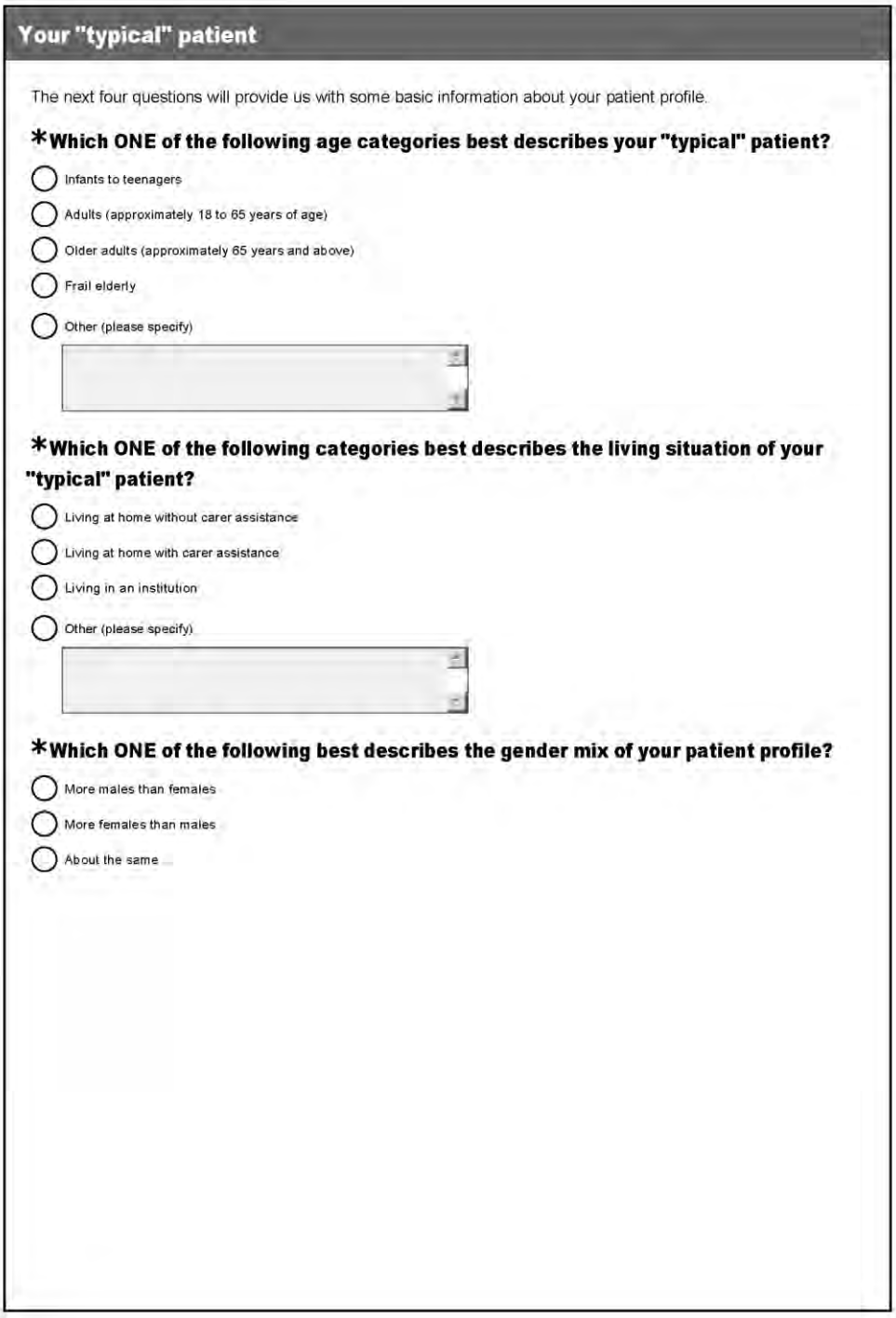
I understand that the results of this study may be published in medical literature, and if my responses are used in any publication/s resulting from this research, they will be suitably de-identified.

I also understand that I may withdraw from the study at any point in time by notifying the research team.

***I consent and agree to the above**

◯ Yes

This study has been approved by the Tasmanian Social Sciences Human Research Ethics Committee. If you have concerns or complaints about the conduct of this study you should contact the Executive Officer of the HREC (Tasmania) Network on (03) 6226 7479 or email human.ethics@utas.edu.au. The Executive Officer is the person nominated to receive complaints from research participants. You will need to quote HREC project number H9360.



Your "typical" patient

The next four questions will provide us with some basic information about your patient profile.

***Which ONE of the following age categories best describes your "typical" patient?**

- ◯ Infants to teenagers
- ◯ Adults (approximately 18 to 65 years of age)
- ◯ Older adults (approximately 65 years and above)
- ◯ Frail elderly
- ◯ Other (please specify)

***Which ONE of the following categories best describes the living situation of your "typical" patient?**

- ◯ Living at home without carer assistance
- ◯ Living at home with carer assistance
- ◯ Living in an institution
- ◯ Other (please specify)

***Which ONE of the following best describes the gender mix of your patient profile?**

- ◯ More males than females
- ◯ More females than males
- ◯ About the same

Please indicate which of the following, if any, are areas of specialty interest to you?

☐ Andrology	☐ Hepatology	☐ Psychiatry
☐ Angiology	☐ Immunology	☐ Pulmonology
☐ Cardiology	☐ Infectious diseases	☐ Radiology
☐ Dermatology	☐ Nephrology	☐ Rehabilitation medicine
☐ Endocrinology	☐ Neurology	☐ Rheumatology
☐ Gastroenterology	☐ Oncology	☐ Sexual health
☐ Geriatrics	☐ Ophthalmology	☐ Sports medicine
☐ Gerontology	☐ Otolaryngology	☐ Urology
☐ Gynecology/Obstetrics	☐ Palliative medicine	
☐ Haematology	☐ Pediatrics	

Other (please specify)

Appendix XV - Consequences study participant information booklet

PROMISe VALMER

Consequences Study Participant Guide

UMORE Unit for Medication Outcomes Research and Education

Introduction

Researchers at the School of Pharmacy, University of Tasmania, are developing a technique to model the outcomes of interventions made by community pharmacists. This model involves the assigning of ***consequences*** that may occur as a result of an intervention. Your participation in this study will assist the research team to "value" several parameters that describe each of these consequences.

Defining *consequences*

The fundamental premise of this study is that any clinical intervention is associated with numerous potential consequences. Each of these consequences may be either beneficial or detrimental to a patient's health. Ideally, the net effect of all the consequences associated with any intervention will be positive, resulting in a benefit to a patient's health.

For example, consider the following scenario:

- a patient with chronic atrial fibrillation is commenced on warfarin to prevent complications relating to thromboembolism

One potential beneficial consequence of this intervention is a reduction in the risk of cerebrovascular events, whilst a detrimental consequence is an increase in the risk of bleeding.

Both "cerebrovascular events" and "bleeding" are broad terms that encompass a spectrum of severity. For this study, we have defined three ***levels of severity*** for each consequence, termed *mild*, *moderate* and *severe*. Using the consequence of "bleeding" as an example, each severity level has been described as follows:

Severity level	Description
Mild	Easy bruising, bleeding from small cuts, petechia, ecchymosis, mild elevation of INR not requiring adjustment of dosage
Moderate	Haematoma, epistaxis, blood loss from mouth, vagina, melaena, eye bleed, haematuria, haematemesis, moderate elevation of INR requiring modification of dose of anticoagulant
Severe	Bleeding requiring hospitalisation, blood product and/or haemodynamic support

Table 1 - Three severity levels of "bleeding"

Costs of consequences

Most of these consequences will require some degree of medical management to resolve (termed *health-resource utilisation*). It is likely that the management of each severity level of each consequence will require a different degree of health-resource utilisation. For the purposes of this study, we are interested in quantifying three items of health resource utilisation:

- the NUMBER of GENERAL PRACTITIONER visits,
- the NUMBER of SPECIALIST visits, and
- the INVESTIGATIONS (laboratory or otherwise) that would be performed to resolve the consequence.

The aim of this study is to quantify the potential health-resource utilisation of each severity level of each consequence. Participation involves providing your opinion regarding these parameters for sixty consequences at the three severity levels. Essentially, you are answering the question, "If a patient presented to me with this particular problem (i.e. consequence), what would I expect to occur for the problem to be resolved, for up to the next 12 months?". Some of the consequences (especially at mild severity levels) may not require any management whatsoever to resolve; most, however, will require at least one visit to a general practitioner.

It is acknowledged that many factors may influence the health-resource utilisation of these consequences in certain patients - for example, the presence of comorbidities or extremes of age may necessitate more intensive management of each consequence. Please provide your opinions for each consequence based on your typical patients. The data we are collecting is therefore based on your experience; there is no "correct" answer for any of the fields.

The description of the severe level of many of the consequences may include a patient being hospitalised. For this study, we are only investigating health resource utilisation outside hospital (we will be using Australian Hospital Statistics data to quantify hospitalisation). If a consequence involves hospitalisation, please assess the total number of GP/specialist visits and investigations that you would expect to occur outside of the patient being hospitalised.

Duration of each consequence

In addition to the health-resource utilisation of each consequence, you are also asked quantify how many *days of ill health* you would expect the consequence to cause at each level of severity. The timeframe for your projections is 12 months; hence the question you are answering here is, "If a patient presented to me with one occurrence of this particular problem (i.e. consequence), how many days of ill health would I expect them to experience in the next 12 months because of it?". Some consequences may result in a very limited duration of illness (perhaps as short as a few days), and some may cause ongoing illness for the full 12 months. If a consequence results in hospitalisation, please include the expected time hospitalised in your assessment of the duration of the consequence.

How to participate

Participation involves completing three online surveys. Please answer the "days of ill health" and "number of GP/specialist visits" questions using numbers only. "Likely investigations" may be answered in the format of your choice- please indicate what investigations you would perform and the number of times you would perform them to resolve the consequence (throughout the duration of "ill health" caused by that consequence). Leave fields blank where appropriate if you believe no GP visits, specialist visits, or investigations would be required. It is assumed that every level of every consequence will result in some "days of ill health", so a response is always required for this field.

A comments box is also available for each consequence- please use this field to make any comments as appropriate.

To participate in this study, the surveys may be accessed at www.valmer.com.au using the password: Umore

Each survey should take approximately 30 to 60 minutes to complete, and you will be reimbursed $500 once all three surveys are completed. At the conclusion of the study, it may be necessary for us to contact you to clarify your responses if they are unclear. Once you have completed all three surveys, please send a computer-generated invoice for $500 (plus GST if appropriate) to:

VALMER Study
Private Bag 26
University of Tasmania Hobart 7001

Please ensure that your invoice contains your ABN and the words "TAX INVOICE"; if you do not have an ABN, please also fill in an ATO Hobby Declaration (available from this link).

Thank you for your interest. Please contact Andrew Stafford at the University of Tasmania (andrews5@utas.edu.au or 03 6226 1715) if you require any further information.

This study has been approved by the Tasmanian Social Sciences Human Research Ethics Committee. If you have concerns or complaints about the conduct of this study you should contact the Executive Officer of the HREC (Tasmania) Network on (03) 6226 7479 or email human.ethics@utas.edu.au. The Executive Officer is the person nominated to receive complaints from research participants. You will need to quote HREC project number H9360.

Appendix XVI - Consequences study results - pathology and laboratory investigations

TABLE 146 - INVESTIGATIONS ORDERED ACCORDING TO HEALTH STATE AND PERCENTAGE OF EXPERTS THAT SELECTED THEM

CONSEQUENCE SEVERITY LEVEL	INVESTIGATIONS ORDERED DURING RESOLUTION OF HEALTH STATE (% OF EXPERTS SELECTING*)
Acidosis	
Mild	Blood glucose level (18.2%), Electrocardiogram (9.1%), Full blood examination (36.4%), Liver function tests (9.1%), Serum urea, electrolytes and creatinine (63.6%)
Moderate	Arterial blood gasses (45.5%), Blood glucose level (27.3%), Serum calcium and phosphate (18.2%), Chest X-ray (27.3%), Coagulation studies (9.1%), Electrocardiogram (18.2%), Full blood examination (72.7%), Liver function tests (18.2%), Renal ultrasound (9.1%), Spirometry (9.1%), Serum urea, electrolytes and creatinine (100.0%), Urine microscopy, culture and sensitivities (18.2%)
Severe	Arterial blood gasses (72.7%), Blood cultures (9.1%), Blood glucose level (27.3%), Serum calcium and phosphate (9.1%), Chest X-ray (36.4%), Coagulation studies (9.1%), Electrocardiogram (9.1%), Full blood examination (63.6%), Liver function tests (18.2%), Spirometry (9.1%), Serum urea, electrolytes and creatinine (90.9%), Urine microscopy, culture and sensitivities (18.2%)
Alkalosis	
Mild	Blood glucose level (9.1%), Serum calcium and phosphate (9.1%), Chest X-ray (18.2%), Electrocardiogram (9.1%), Full blood examination (63.6%), Liver function tests (27.3%), Serum urea, electrolytes and creatinine (81.8%), Urine microscopy, culture and sensitivities (9.1%)
Moderate	Arterial blood gasses (27.3%), Blood glucose level (9.1%), Chest X-ray (18.2%), Electrocardiogram (9.1%), Faeces microscopy, culture and sensitivities (9.1%), Full blood examination (72.7%), Liver function tests (18.2%), Serum urea, electrolytes and creatinine (100.0%), Urine microscopy, culture and sensitivities (18.2%)
Severe	Arterial blood gasses (27.3%), Chest X-ray (9.1%), Computed tomography head (9.1%), Electrocardiogram (9.1%), Faeces microscopy, culture and sensitivities (9.1%), Full blood examination (72.7%), Liver function tests (9.1%), Spirometry (9.1%), Serum urea, electrolytes and creatinine (81.8%), Urine microscopy, culture and sensitivities (27.3%)
Allergic reaction	
Mild	Nil
Moderate	Full blood examination (18.2%), IgE detection (36.4%), Liver function tests (9.1%), Serum urea, electrolytes and creatinine (9.1%)
Severe	Electrocardiogram (9.1%), Full blood examination (36.4%), IgE detection (72.7%), Liver function tests (9.1%), Skin biopsy (9.1%), Serum urea, electrolytes and creatinine (45.5%)
Anaemia	
Mild	Serum B12 and folate (27.3%), Colonoscopy (9.1%), Electrocardiogram (9.1%), Faecal occult blood (18.2%), Full blood examination (100.0%), Iron studies (54.5%), Liver function tests (9.1%), Thyroid function tests (18.2%), Serum urea, electrolytes and creatinine (63.6%)

CONSEQUENCE SEVERITY LEVEL	INVESTIGATIONS ORDERED DURING RESOLUTION OF HEALTH STATE (% OF EXPERTS SELECTING*)
Moderate	Serum B12 and folate (54.5%), Bone marrow biopsy (18.2%), Chest X-ray (9.1%), Colonoscopy (54.5%), Electrocardiogram (9.1%), Endoscopy (63.6%), Faecal occult blood (36.4%), Full blood examination (100.0%), Iron studies (63.6%), Liver function tests (18.2%), Thyroid function tests (18.2%), Serum urea, electrolytes and creatinine (72.7%), Urine microscopy, culture and sensitivities (9.1%)
Severe	Serum B12 and folate (45.5%), Bone marrow biopsy (36.4%), Chest X-ray (9.1%), Colonoscopy (72.7%), Electrocardiogram (9.1%), Endoscopy (90.9%), Full blood examination (81.8%), Iron studies (36.4%), Liver function tests (9.1%), Thyroid function tests (9.1%), Serum urea, electrolytes and creatinine (54.5%)
Anxiety	
Mild	Electrocardiogram (9.1%), Full blood examination (9.1%), Serum urea, electrolytes and creatinine (9.1%)
Moderate	Blood glucose level (9.1%), Electrocardiogram (18.2%), Full blood examination (63.6%), Liver function tests (18.2%), Parathyroid hormone (9.1%), Thyroid function tests (54.5%), Serum urea, electrolytes and creatinine (63.6%)
Severe	Blood glucose level (9.1%), Electrocardiogram (9.1%), Electroencephalogram (9.1%), Full blood examination (54.5%), Iron studies (9.1%), Liver function tests (9.1%), Thyroid function tests (45.5%), Serum urea, electrolytes and creatinine (63.6%), Urine microscopy, culture and sensitivities (9.1%)
Arrhythmia	
Mild	Blood glucose level (9.1%), Serum calcium and phosphate (27.3%), Chest X-ray (9.1%), Creatine kinase (9.1%), Electrocardiogram (100.0%), Full blood examination (63.6%), Iron studies (9.1%), Lipid studies (9.1%), Thyroid function tests (27.3%), Serum urea, electrolytes and creatinine (72.7%)
Moderate	Angiography (9.1%), Blood glucose level (9.1%), Serum calcium and phosphate (18.2%), Chest X-ray (45.5%), Creatine kinase (9.1%), Echocardiogram (36.4%), Electrocardiogram (100.0%), Full blood examination (81.8%), Lipid studies (9.1%), Thyroid function tests (27.3%), Serum urea, electrolytes and creatinine (81.8%)
Severe	Angiography (27.3%), Serum calcium and phosphate (9.1%), Chest X-ray (18.2%), Creatine kinase (18.2%), Echocardiogram (36.4%), Electrocardiogram (81.8%), Full blood examination (72.7%), Thyroid function tests (18.2%), Serum urea, electrolytes and creatinine (72.7%)
Asthma	
Mild	Spirometry (36.4%),
Moderate	Arterial blood gasses (9.1%), Chest X-ray (18.2%), Full blood examination (9.1%), Spirometry (63.6%), Sputum microscopy, culture and sensitivities (9.1%), Serum urea, electrolytes and creatinine (9.1%)
Severe	Arterial blood gasses (63.6%), Blood cultures (9.1%), Chest X-ray (90.9%), Electrocardiogram (9.1%), Full blood examination (54.5%), Spirometry (63.6%), Sputum microscopy, culture and sensitivities (27.3%), Serum urea, electrolytes and creatinine (54.5%),
Bleeding, non-specific	
Mild	Coagulation studies (72.7%), Electrocardiogram (9.1%), Full blood examination (72.7%), Liver function tests (27.3%), Serum urea, electrolytes and creatinine (45.5%), Urine microscopy, culture and sensitivities (9.1%)
Moderate	Abdominal ultrasound (9.1%), Coagulation studies (72.7%), Colonoscopy (27.3%), Electrocardiogram (9.1%), Endoscopy (45.5%), Faecal occult blood (9.1%), Full blood examination (90.9%), Iron studies (18.2%), Liver function tests (27.3%), Renal ultrasound (9.1%), Serum urea, electrolytes and creatinine (72.7%), Urine microscopy, culture and sensitivities (9.1%)
Severe	Abdominal ultrasound (9.1%), Coagulation studies (54.5%), Colonoscopy (27.3%), Computed tomography head (9.1%), Electrocardiogram (9.1%), Endoscopy (45.5%), Faecal occult blood (9.1%), Full blood examination (81.8%), Iron studies (9.1%), Liver function tests (27.3%), Renal ultrasound (9.1%), Serum urea, electrolytes and creatinine (63.6%), Urine

CONSEQUENCE SEVERITY LEVEL	INVESTIGATIONS ORDERED DURING RESOLUTION OF HEALTH STATE (% OF EXPERTS SELECTING*)
	microscopy, culture and sensitivities (9.1%)
Bone marrow suppression	
Mild	Serum B12 and folate (18.2%), Blood cultures (9.1%), Coagulation studies (9.1%), Full blood examination (90.9%), Iron studies (18.2%), Liver function tests (27.3%), Thyroid function tests (9.1%), Serum urea, electrolytes and creatinine (72.7%)
Moderate	Abdominal ultrasound (9.1%), Serum B12 and folate (18.2%), Bone marrow biopsy (18.2%), Chest X-ray (9.1%), Coagulation studies (9.1%), Dual energy X-ray absorptiometry (9.1%), Full blood examination (90.9%), Iron studies (18.2%), Liver function tests (27.3%), Thyroid function tests (9.1%), Serum urea, electrolytes and creatinine (72.7%)
Severe	Abdominal ultrasound (9.1%), Serum B12 and folate (18.2%), Bone marrow biopsy (90.9%), Chest X-ray (9.1%), Dual energy X-ray absorptiometry (18.2%), Full blood examination (90.9%), Iron studies (18.2%), Liver function tests (27.3%), Thyroid function tests (9.1%), Serum urea, electrolytes and creatinine (63.6%
Cerebrovascular event	
Mild	Blood glucose level (18.2%), Carotid doppler (72.7%), Chest X-ray (9.1%), Computed tomography head (63.6%), Creatine kinase (9.1%), Echocardiogram (54.5%), Electrocardiogram (54.5%), Full blood examination (81.8%), Lipid studies (9.1%), Thyroid function tests (9.1%), Serum urea, electrolytes and creatinine (72.7%), Urine microscopy, culture and sensitivities (9.1%)
Moderate	Blood glucose level (9.1%), Carotid doppler (63.6%), Chest X-ray (9.1%), Computed tomography head (90.9%), Creatine kinase (9.1%), Echocardiogram (54.5%), Electrocardiogram (63.6%), Full blood examination (81.8%), Thyroid function tests (9.1%), Serum urea, electrolytes and creatinine (72.7%)
Severe	Angiography (18.2%), Blood glucose level (9.1%), Carotid doppler (72.7%), Chest X-ray (9.1%), Coagulation studies (9.1%), Computed tomography head (81.8%), Creatine kinase (9.1%), Echocardiogram (54.5%), Electrocardiogram (63.6%), Full blood examination (81.8%), Magnetic resonance imaging (head) (18.2%), Thyroid function tests (9.1%), Serum urea, electrolytes and creatinine (63.6%)
Chronic Airways Disease	
Mild	Arterial blood gasses (9.1%), Chest X-ray (18.2%), Full blood examination (18.2%), Liver function tests (9.1%), Spirometry (72.7%), Serum urea, electrolytes and creatinine (9.1%)
Moderate	Arterial blood gasses (9.1%), Blood cultures (9.1%), Chest X-ray (72.7%), Electrocardiogram (9.1%), Full blood examination (54.5%), Liver function tests (9.1%), Spirometry (81.8%), Sputum microscopy, culture and sensitivities (18.2%), Serum urea, electrolytes and creatinine (45.5%)
Severe	Arterial blood gasses (54.5%), Blood cultures (9.1%), Chest X-ray (81.8%), Electrocardiogram (9.1%), Full blood examination (72.7%), Liver function tests (18.2%), Spirometry (81.8%), Sputum microscopy, culture and sensitivities (18.2%), Serum urea, electrolytes and creatinine (63.6%)
CNS Depression	
Mild	Serum B12 and folate (18.2%), Computed tomography head (9.1%), Electrocardiogram (9.1%), Full blood examination (36.4%), Iron studies (18.2%), Thyroid function tests (27.3%), Serum urea, electrolytes and creatinine (36.4%), Urine microscopy, culture and sensitivities (9.1%)
Moderate	Arterial blood gasses (9.1%), Serum B12 and folate (18.2%), Blood cultures (9.1%), Blood glucose level (27.3%), Serum calcium and phosphate (9.1%), Computed tomography head (36.4%), Electrocardiogram (18.2%), Full blood examination (81.8%), Iron studies (18.2%), Liver function tests (18.2%), Magnetic resonance imaging (head) (9.1%), Thyroid function tests (45.5%), Serum urea, electrolytes and creatinine (72.7%), Urine microscopy, culture and sensitivities (18.2%)
Severe	Arterial blood gasses (45.5%), Serum B12 and folate (27.3%), Blood cultures (9.1%), Blood glucose level (27.3%), Serum calcium and phosphate (9.1%), Computed tomography head

CONSEQUENCE SEVERITY LEVEL	INVESTIGATIONS ORDERED DURING RESOLUTION OF HEALTH STATE (% OF EXPERTS SELECTING*)
	(54.5%), Electrocardiogram (18.2%), Electroencephalogram (9.1%), Full blood examination (81.8%), Iron studies (18.2%), Liver function tests (18.2%), Magnetic resonance imaging (head) (18.2%), Thyroid function tests (45.5%), Serum urea, electrolytes and creatinine (72.7%), Urine microscopy, culture and sensitivities (27.3%)
Confusion	
Mild	Arterial blood gasses (9.1%), Serum B12 and folate (9.1%), Blood glucose level (18.2%), Chest X-ray (9.1%), Computed tomography head (18.2%), Electrocardiogram (9.1%), Full blood examination (72.7%), Liver function tests (27.3%), Thyroid function tests (27.3%), Serum urea, electrolytes and creatinine (72.7%), Urine microscopy, culture and sensitivities (36.4%)
Moderate	Serum B12 and folate (27.3%), Blood glucose level (18.2%), Serum calcium and phosphate (9.1%), Chest X-ray (27.3%), Computed tomography head (54.5%), Electrocardiogram (9.1%), Full blood examination (90.9%), Iron studies (9.1%), Liver function tests (27.3%), Thyroid function tests (18.2%), Serum urea, electrolytes and creatinine (90.9%), Urine microscopy, culture and sensitivities (72.7%)
Severe	Serum B12 and folate (18.2%), Blood glucose level (18.2%), Serum calcium and phosphate (9.1%), Chest X-ray (36.4%), Computed tomography head (81.8%), Electrocardiogram (9.1%), Electroencephalogram (18.2%), Full blood examination (81.8%), Liver function tests (18.2%), Magnetic resonance imaging (head) (9.1%), Thyroid function tests (18.2%), Serum urea, electrolytes and creatinine (81.8%), Urine microscopy, culture and sensitivities (63.6%)
Constipation	
Mild	Nil
Moderate	Abdominal X-ray (36.4%), Serum calcium and phosphate (18.2%), Colonoscopy (9.1%), Full blood examination (45.5%), Thyroid function tests (18.2%), Serum urea, electrolytes and creatinine (45.5%)
Severe	Abdominal X-ray (54.5%), Arterial blood gasses (9.1%), Serum calcium and phosphate (27.3%), Chest X-ray (9.1%), Colonoscopy (81.8%), Full blood examination (54.5%), Thyroid function tests (18.2%), Serum urea, electrolytes and creatinine (63.6%), Urine microscopy, culture and sensitivities (9.1%)
Dementia	
Mild	Serum B12 and folate (36.4%), Blood glucose level (9.1%), Serum calcium and phosphate (9.1%), Chest X-ray (9.1%), Computed tomography head (54.5%), Full blood examination (63.6%), Iron studies (9.1%), Liver function tests (27.3%), Thyroid function tests (36.4%), Serum urea, electrolytes and creatinine (72.7%), Urine microscopy, culture and sensitivities (54.5%)
Moderate	Serum B12 and folate (45.5%), Blood cultures (9.1%), Blood glucose level (27.3%), Serum calcium and phosphate (18.2%), Chest X-ray (18.2%), Computed tomography head (63.6%), Echocardiogram (9.1%), Full blood examination (72.7%), Iron studies (9.1%), Lipid studies (9.1%), Liver function tests (36.4%), Magnetic resonance imaging (head) (9.1%), Thyroid function tests (45.5%), Serum urea, electrolytes and creatinine (81.8%), Urine microscopy, culture and sensitivities (63.6%)
Severe	Serum B12 and folate (36.4%), Blood glucose level (18.2%), Serum calcium and phosphate (9.1%), Chest X-ray (9.1%), Computed tomography head (81.8%), Echocardiogram (9.1%), Full blood examination (63.6%), Iron studies (9.1%), Liver function tests (27.3%), Magnetic resonance imaging (head) (18.2%), Thyroid function tests (36.4%), Serum urea, electrolytes and creatinine (72.7%), Urine microscopy, culture and sensitivities (54.5%)
Depression	
Mild	Serum B12 and folate (9.1%), Full blood examination (27.3%), Thyroid function tests (18.2%), Serum urea, electrolytes and creatinine (36.4%),

CONSEQUENCE SEVERITY LEVEL	INVESTIGATIONS ORDERED DURING RESOLUTION OF HEALTH STATE (% OF EXPERTS SELECTING*)
Moderate	Serum B12 and folate (36.4%), Blood cultures (9.1%), Blood glucose level (27.3%), Serum calcium and phosphate (18.2%), Full blood examination (72.7%), Iron studies (9.1%), Liver function tests (18.2%), Thyroid function tests (63.6%), Serum urea, electrolytes and creatinine (72.7%),
Severe	Serum B12 and folate (27.3%), Blood glucose level (27.3%), Serum calcium and phosphate (9.1%), Computed tomography head (27.3%), Full blood examination (72.7%), Liver function tests (18.2%), Magnetic resonance imaging (head) (9.1%), Thyroid function tests (54.5%), Serum urea, electrolytes and creatinine (81.8%), Urine microscopy, culture and sensitivities (18.2%)
Diabetes	
Mild	Albumin: creatinine ratio (18.2%), Blood glucose level (54.5%), Chest X-ray (18.2%), Full blood examination (45.5%), Glycosylated haemoglobin (36.4%), Lipid studies (9.1%), Liver function tests (18.2%), Thyroid function tests (9.1%), Serum urea, electrolytes and creatinine (54.5%), Urine microscopy, culture and sensitivities (36.4%)
Moderate	Albumin: creatinine ratio (18.2%), Blood cultures (9.1%), Blood glucose level (45.5%), Chest X-ray (36.4%), Full blood examination (72.7%), Glycosylated haemoglobin (36.4%), Lipid studies (9.1%), Liver function tests (27.3%), Thyroid function tests (9.1%), Serum urea, electrolytes and creatinine (100.0%), Urine microscopy, culture and sensitivities (54.5%)
Severe	Albumin: creatinine ratio (18.2%), Arterial blood gasses (27.3%), Blood cultures (18.2%), Blood glucose level (45.5%), Chest X-ray (45.5%), Coagulation studies (9.1%), Full blood examination (72.7%), Glycosylated haemoglobin (36.4%), Lipid studies (9.1%), Liver function tests (18.2%), Thyroid function tests (9.1%), Serum urea, electrolytes and creatinine (100.0%), Urine microscopy, culture and sensitivities (63.6%)
Diarrhoea	
Mild	Nil
Moderate	Abdominal X-ray (18.2%), Serum B12 and folate (9.1%), Blood cultures (9.1%), Blood glucose level (9.1%), Colonoscopy (9.1%), Faeces microscopy, culture and sensitivities (63.6%), Full blood examination (45.5%), Iron studies (9.1%), Liver function tests (27.3%), Thyroid function tests (9.1%), Serum urea, electrolytes and creatinine (54.5%)
Severe	Abdominal X-ray (9.1%), Arterial blood gasses (9.1%), Serum B12 and folate (9.1%), Blood cultures (9.1%), Blood glucose level (9.1%), Colonoscopy (9.1%), Endoscopy (9.1%), Faeces microscopy, culture and sensitivities (72.7%), Full blood examination (72.7%), Liver function tests (18.2%), Serum urea, electrolytes and creatinine (90.9%)
Gastrointestinal bleeding	
Mild	Colonoscopy (18.2%), Endoscopy (18.2%), Faecal occult blood (36.4%), Full blood examination (45.5%), Iron studies (9.1%), Liver function tests (9.1%), Serum urea, electrolytes and creatinine (27.3%)
Moderate	Chest X-ray (9.1%), Coagulation studies (9.1%), Colonoscopy (63.6%), Endoscopy (63.6%), Faecal occult blood (9.1%), Full blood examination (90.9%), Iron studies (27.3%), Liver function tests (45.5%), Serum urea, electrolytes and creatinine (81.8%)
Severe	Arterial blood gasses (9.1%), Chest X-ray (27.3%), Coagulation studies (9.1%), Colonoscopy (54.5%), Electrocardiogram (18.2%), Endoscopy (81.8%), Faecal occult blood (9.1%), Full blood examination (72.7%), Iron studies (18.2%), Liver function tests (36.4%), Serum urea, electrolytes and creatinine (63.6%)
Gastrointestinal pain	
Mild	Nil
Moderate	Abdominal ultrasound (18.2%), Abdominal X-ray (9.1%), Chest X-ray (9.1%), Colonoscopy (9.1%), Endoscopy (18.2%), Faeces microscopy, culture and sensitivities (9.1%), Full blood examination (72.7%), Iron studies (9.1%), Liver function tests (27.3%), Serum urea, electrolytes and creatinine (54.5%)

CONSEQUENCE SEVERITY LEVEL	INVESTIGATIONS ORDERED DURING RESOLUTION OF HEALTH STATE (% OF EXPERTS SELECTING*)
Severe	Abdominal ultrasound (36.4%), Abdominal X-ray (9.1%), Blood cultures (9.1%), Chest X-ray (9.1%), Colonoscopy (27.3%), Computed tomography head (9.1%), Endoscopy (54.5%), Faeces microscopy, culture and sensitivities (27.3%), Full blood examination (90.9%), Iron studies (9.1%), Liver function tests (45.5%), Serum urea, electrolytes and creatinine (72.7%), Urine microscopy, culture and sensitivities (9.1%)
Glaucoma	
Mild	Full blood examination (9.1%), Low vision assessment (36.4%), Serum urea, electrolytes and creatinine (9.1%)
Moderate	Blood glucose level (9.1%), Full blood examination (18.2%), Low vision assessment (54.5%), Serum urea, electrolytes and creatinine (9.1%)
Severe	Blood glucose level (9.1%), Computed tomography head (9.1%), Full blood examination (27.3%), Low vision assessment (45.5%), Serum urea, electrolytes and creatinine (27.3%)
Headache	
Mild	
Moderate	Blood glucose level (9.1%), Computed tomography head (18.2%), Full blood examination (18.2%), Liver function tests (9.1%), Serum urea, electrolytes and creatinine (9.1%)
Severe	Blood cultures (9.1%), Blood glucose level (9.1%), Computed tomography head (100.0%), Full blood examination (54.5%), Liver function tests (27.3%), Serum urea, electrolytes and creatinine (54.5%), Urine microscopy, culture and sensitivities (9.1%)
Heart Failure	
Mild	Blood glucose level (9.1%), Chest X-ray (63.6%), Creatine kinase (9.1%), Echocardiogram (36.4%), Electrocardiogram (54.5%), Full blood examination (63.6%), Liver function tests (27.3%), Thyroid function tests (18.2%), Serum urea, electrolytes and creatinine (63.6%)
Moderate	Angiography (9.1%), Blood glucose level (9.1%), Chest X-ray (81.8%), Creatine kinase (9.1%), Echocardiogram (54.5%), Electrocardiogram (81.8%), Full blood examination (81.8%), Liver function tests (27.3%), Thyroid function tests (18.2%), Serum urea, electrolytes and creatinine (90.9%)
Severe	Angiography (9.1%), Arterial blood gasses (9.1%), Blood glucose level (9.1%), Chest X-ray (81.8%), Creatine kinase (9.1%), Echocardiogram (63.6%), Electrocardiogram (72.7%), Full blood examination (72.7%), Liver function tests (27.3%), Thyroid function tests (27.3%), Serum urea, electrolytes and creatinine (72.7%)
Hypercalcaemia	
Mild	Blood glucose level (9.1%), Serum calcium and phosphate (45.5%), Full blood examination (45.5%), Liver function tests (9.1%), Parathyroid hormone (27.3%), Thyroid function tests (18.2%), Serum urea, electrolytes and creatinine (72.7%), Vitamin D (9.1%)
Moderate	Arterial blood gasses (9.1%), Blood glucose level (18.2%), Serum calcium and phosphate (63.6%), Chest X-ray (18.2%), Creatine kinase (9.1%), Electrocardiogram (9.1%), Full blood examination (54.5%), Liver function tests (27.3%), Parathyroid hormone (54.5%), Renal ultrasound (9.1%), Thyroid function tests (36.4%), Serum urea, electrolytes and creatinine (90.9%), Urine microscopy, culture and sensitivities (9.1%), Vitamin D (9.1%)
Severe	Arterial blood gasses (18.2%), Blood glucose level (18.2%), Serum calcium and phosphate (45.5%), Chest X-ray (18.2%), Dual energy X-ray absorptiometry (18.2%), Full blood examination (36.4%), Liver function tests (9.1%), Parathyroid hormone (45.5%), Renal ultrasound (9.1%), Thyroid function tests (18.2%), Serum urea, electrolytes and creatinine (63.6%), Urine microscopy, culture and sensitivities (9.1%)

CONSEQUENCE SEVERITY LEVEL	INVESTIGATIONS ORDERED DURING RESOLUTION OF HEALTH STATE (% OF EXPERTS SELECTING*)
Hyperkalaemia	
Mild	Blood glucose level (9.1%), Full blood examination (45.5%), Liver function tests (9.1%), Serum urea, electrolytes and creatinine (90.9%)
Moderate	Blood glucose level (18.2%), Coagulation studies (9.1%), Electrocardiogram (72.7%), Full blood examination (63.6%), Liver function tests (27.3%), Thyroid function tests (9.1%), Serum urea, electrolytes and creatinine (100.0%), Urine microscopy, culture and sensitivities (18.2%)
Severe	Arterial blood gasses (18.2%), Blood cultures (9.1%), Blood glucose level (18.2%), Chest X-ray (18.2%), Coagulation studies (9.1%), Electrocardiogram (63.6%), Full blood examination (54.5%), Liver function tests (9.1%), Renal ultrasound (18.2%), Thyroid function tests (9.1%), Serum urea, electrolytes and creatinine (90.9%), Urine microscopy, culture and sensitivities (27.3%)
Hypertension	
Mild	Blood glucose level (18.2%), Electrocardiogram (18.2%), Full blood examination (45.5%), Lipid studies (18.2%), Liver function tests (18.2%), Thyroid function tests (9.1%), Serum urea, electrolytes and creatinine (63.6%), Urine microscopy, culture and sensitivities (9.1%)
Moderate	Blood glucose level (18.2%), Chest X-ray (27.3%), Echocardiogram (36.4%), Electrocardiogram (63.6%), Full blood examination (72.7%), Lipid studies (18.2%), Liver function tests (18.2%), Renal ultrasound (18.2%), Thyroid function tests (9.1%), Serum urea, electrolytes and creatinine (100.0%), Urine microscopy, culture and sensitivities (27.3%)
Severe	Albumin: creatinine ratio (9.1%), Angiography (9.1%), Blood glucose level (18.2%), Chest X-ray (27.3%), Computed tomography head (18.2%), Echocardiogram (45.5%), Electrocardiogram (54.5%), Full blood examination (63.6%), Lipid studies (18.2%), Liver function tests (9.1%), Renal ultrasound (9.1%), Thyroid function tests (9.1%), Serum urea, electrolytes and creatinine (90.9%), Urine microscopy, culture and sensitivities (27.3%)
Hyperthyroidism	
Mild	Electrocardiogram (9.1%), Full blood examination (54.5%), Liver function tests (18.2%), Thyroid function tests (72.7%), Serum urea, electrolytes and creatinine (54.5%)
Moderate	Serum calcium and phosphate (9.1%), Electrocardiogram (18.2%), Full blood examination (72.7%), Liver function tests (27.3%), Thyroid function tests (72.7%), Serum urea, electrolytes and creatinine (72.7%)
Severe	Serum calcium and phosphate (9.1%), Electrocardiogram (27.3%), Full blood examination (72.7%), Liver function tests (27.3%), Thyroid function tests (72.7%), Serum urea, electrolytes and creatinine (72.7%)
Hypocalcaemia	
Mild	Serum calcium and phosphate (45.5%), Electrocardiogram (18.2%), Full blood examination (63.6%), Liver function tests (18.2%), Parathyroid hormone (36.4%), Thyroid function tests (27.3%), Serum urea, electrolytes and creatinine (72.7%), Vitamin D (9.1%)
Moderate	Arterial blood gasses (9.1%), Serum calcium and phosphate (45.5%), Electrocardiogram (54.5%), Full blood examination (63.6%), Liver function tests (18.2%), Parathyroid hormone (45.5%), Thyroid function tests (36.4%), Serum urea, electrolytes and creatinine (81.8%), Urine microscopy, culture and sensitivities (9.1%), Vitamin D (9.1%)
Severe	Arterial blood gasses (27.3%), Serum calcium and phosphate (45.5%), Dual energy X-ray absorptiometry (9.1%), Electrocardiogram (63.6%), Full blood examination (63.6%), Liver function tests (18.2%), Parathyroid hormone (45.5%), Renal ultrasound (9.1%), Thyroid function tests (36.4%), Serum urea, electrolytes and creatinine (81.8%), Urine microscopy, culture and sensitivities (9.1%), Vitamin D (9.1%)
Hypoglycaemia	

CONSEQUENCE SEVERITY LEVEL	INVESTIGATIONS ORDERED DURING RESOLUTION OF HEALTH STATE (% OF EXPERTS SELECTING*)
Mild	Blood glucose level (63.6%), Full blood examination (27.3%), Glycosylated haemoglobin (36.4%), Serum urea, electrolytes and creatinine (36.4%), Urine microscopy, culture and sensitivities (9.1%)
Moderate	Abdominal ultrasound (9.1%), Albumin: creatinine ratio (9.1%), Blood glucose level (72.7%), Computed tomography head (9.1%), Electrocardiogram (9.1%), Full blood examination (45.5%), Glycosylated haemoglobin (54.5%), Liver function tests (9.1%), Thyroid function tests (9.1%), Serum urea, electrolytes and creatinine (63.6%), Urine microscopy, culture and sensitivities (27.3%)
Severe	Abdominal ultrasound (9.1%), Albumin: creatinine ratio (9.1%), Arterial blood gasses (27.3%), Blood cultures (9.1%), Blood glucose level (72.7%), Chest X-ray (9.1%), Computed tomography head (9.1%), Electrocardiogram (18.2%), Full blood examination (63.6%), Glycosylated haemoglobin (54.5%), Liver function tests (9.1%), Thyroid function tests (9.1%), Serum urea, electrolytes and creatinine (72.7%), Urine microscopy, culture and sensitivities (27.3%)
Hypokalaemia	
Mild	Electrocardiogram (27.3%), Full blood examination (36.4%), Serum urea, electrolytes and creatinine (81.8%)
Moderate	Arterial blood gasses (9.1%), Serum calcium and phosphate (9.1%), Electrocardiogram (63.6%), Full blood examination (72.7%), Liver function tests (9.1%), Thyroid function tests (9.1%), Serum urea, electrolytes and creatinine (100.0%), Urine microscopy, culture and sensitivities (9.1%)
Severe	Arterial blood gasses (18.2%), Serum calcium and phosphate (9.1%), Echocardiogram (9.1%), Electrocardiogram (72.7%), Full blood examination (63.6%), Liver function tests (9.1%), Thyroid function tests (18.2%), Serum urea, electrolytes and creatinine (90.9%), Urine microscopy, culture and sensitivities (9.1%)
Hypotension	
Mild	Chest X-ray (9.1%), Electrocardiogram (36.4%), Full blood examination (27.3%), Thyroid function tests (9.1%), Serum urea, electrolytes and creatinine (45.5%), Urine microscopy, culture and sensitivities (9.1%)
Moderate	Blood glucose level (9.1%), Chest X-ray (9.1%), Creatine kinase (9.1%), Echocardiogram (9.1%), Electrocardiogram (45.5%), Full blood examination (36.4%), Liver function tests (9.1%), Thyroid function tests (18.2%), Serum urea, electrolytes and creatinine (54.5%), Urine microscopy, culture and sensitivities (9.1%)
Severe	Arterial blood gasses (9.1%), Blood cultures (9.1%), Blood glucose level (9.1%), Chest X-ray (27.3%), Computed tomography head (27.3%), Creatine kinase (9.1%), Echocardiogram (9.1%), Electrocardiogram (63.6%), Full blood examination (63.6%), Liver function tests (18.2%), Thyroid function tests (27.3%), Serum urea, electrolytes and creatinine (81.8%), Urine microscopy, culture and sensitivities (9.1%)
Hypothyroidism	
Mild	Blood glucose level (9.1%), Full blood examination (54.5%), Iron studies (9.1%), Lipid studies (9.1%), Liver function tests (9.1%), Thyroid function tests (63.6%), Serum urea, electrolytes and creatinine (54.5%)
Moderate	Blood glucose level (27.3%), Echocardiogram (9.1%), Electrocardiogram (18.2%), Full blood examination (72.7%), Iron studies (9.1%), Lipid studies (18.2%), Liver function tests (9.1%), Thyroid function tests (72.7%), Serum urea, electrolytes and creatinine (72.7%)
Severe	Blood glucose level (27.3%), Serum calcium and phosphate (9.1%), Echocardiogram (9.1%), Electrocardiogram (18.2%), Full blood examination (72.7%), Iron studies (9.1%), Lipid studies (18.2%), Liver function tests (9.1%), Thyroid function tests (72.7%), Serum urea, electrolytes and creatinine (72.7%)
Infection, general	
Mild	

CONSEQUENCE SEVERITY LEVEL	INVESTIGATIONS ORDERED DURING RESOLUTION OF HEALTH STATE (% OF EXPERTS SELECTING*)
Moderate	Blood cultures (9.1%), Blood glucose level (9.1%), Chest X-ray (63.6%), Full blood examination (63.6%), Liver function tests (18.2%), Sputum microscopy, culture and sensitivities (9.1%), Serum urea, electrolytes and creatinine (54.5%), Urine microscopy, culture and sensitivities (36.4%)
Severe	Arterial blood gasses (27.3%), Blood cultures (54.5%), Blood glucose level (9.1%), Chest X-ray (90.9%), Full blood examination (90.9%), Liver function tests (18.2%), Sputum microscopy, culture and sensitivities (9.1%), Serum urea, electrolytes and creatinine (63.6%), Urine microscopy, culture and sensitivities (45.5%)
Insomnia	
Mild	Nil
Moderate	Electrocardiogram (9.1%), Full blood examination (45.5%), Thyroid function tests (27.3%), Serum urea, electrolytes and creatinine (45.5%)
Severe	Serum B12 and folate (9.1%), Electrocardiogram (9.1%), Full blood examination (45.5%), Iron studies (9.1%), Thyroid function tests (27.3%), Serum urea, electrolytes and creatinine (45.5%)
Liver Disease	
Mild	Abdominal ultrasound (9.1%), Full blood examination (45.5%), Iron studies (9.1%), Liver function tests (45.5%), Serum urea, electrolytes and creatinine (45.5%)
Moderate	Abdominal ultrasound (36.4%), Blood glucose level (18.2%), Coagulation studies (18.2%), Endoscopy (9.1%), Full blood examination (72.7%), Iron studies (27.3%), Liver biopsy (9.1%), Liver function tests (36.4%), Thyroid function tests (9.1%), Serum urea, electrolytes and creatinine (81.8%)
Severe	Abdominal ultrasound (36.4%), Blood glucose level (18.2%), Coagulation studies (18.2%), Endoscopy (9.1%), Full blood examination (72.7%), Iron studies (27.3%), Liver biopsy (27.3%), Liver function tests (36.4%), Thyroid function tests (9.1%), Serum urea, electrolytes and creatinine (81.8%)
Myocardial Ischaemia	
Mild	Blood glucose level (18.2%), Chest X-ray (18.2%), Creatine kinase (18.2%), Echocardiogram (27.3%), Electrocardiogram (63.6%), Full blood examination (72.7%), Lipid studies (18.2%), Liver function tests (9.1%), Thyroid function tests (9.1%), Serum urea, electrolytes and creatinine (72.7%)
Moderate	Angiography (54.5%), Blood glucose level (27.3%), Chest X-ray (36.4%), Creatine kinase (36.4%), Echocardiogram (54.5%), Electrocardiogram (90.9%), Full blood examination (90.9%), Lipid studies (18.2%), Liver function tests (18.2%), Thyroid function tests (18.2%), Serum urea, electrolytes and creatinine (90.9%)
Severe	Angiography (72.7%), Blood glucose level (18.2%), Chest X-ray (54.5%), Creatine kinase (36.4%), Echocardiogram (54.5%), Electrocardiogram (81.8%), Full blood examination (72.7%), Lipid studies (9.1%), Liver function tests (18.2%), Thyroid function tests (18.2%), Serum urea, electrolytes and creatinine (81.8%)
Myopathy	
Mild	Creatine kinase (36.4%), Full blood examination (27.3%), Lipid studies (9.1%), Liver function tests (18.2%), Serum urea, electrolytes and creatinine (27.3%)
Moderate	Blood glucose level (9.1%), Creatine kinase (54.5%), Full blood examination (72.7%), Lipid studies (9.1%), Liver function tests (27.3%), Thyroid function tests (9.1%), Serum urea, electrolytes and creatinine (63.6%)
Severe	Blood glucose level (9.1%), Computed tomography head (9.1%), Creatine kinase (63.6%), Full blood examination (81.8%), Lipid studies (9.1%), Liver function tests (27.3%), Magnetic resonance imaging (head) (9.1%), Thyroid function tests (9.1%), Serum urea, electrolytes and creatinine (72.7%)
Nausea	

CONSEQUENCE SEVERITY LEVEL	INVESTIGATIONS ORDERED DURING RESOLUTION OF HEALTH STATE (% OF EXPERTS SELECTING*)
Mild	Serum urea, electrolytes and creatinine (9.1%),
Moderate	Abdominal ultrasound (9.1%), Abdominal X-ray (9.1%), Blood glucose level (18.2%), Serum calcium and phosphate (9.1%), Full blood examination (63.6%), Liver function tests (27.3%), Serum urea, electrolytes and creatinine (90.9%), Urine microscopy, culture and sensitivities (9.1%)
Severe	Abdominal ultrasound (9.1%), Abdominal X-ray (18.2%), Arterial blood gasses (18.2%), Blood glucose level (18.2%), Serum calcium and phosphate (9.1%), Endoscopy (18.2%), Full blood examination (63.6%), Liver function tests (36.4%), Serum urea, electrolytes and creatinine (100.0%), Urine microscopy, culture and sensitivities (9.1%)
Oedema	
Mild	Chest X-ray (9.1%), Electrocardiogram (9.1%), Full blood examination (9.1%), Serum urea, electrolytes and creatinine (18.2%)
Moderate	Carotid doppler (9.1%), Chest X-ray (72.7%), Coagulation studies (9.1%), Creatine kinase (9.1%), Echocardiogram (27.3%), Electrocardiogram (36.4%), Full blood examination (72.7%), Liver function tests (18.2%), Thyroid function tests (9.1%), Serum urea, electrolytes and creatinine (100.0%), Urine microscopy, culture and sensitivities (9.1%)
Severe	Arterial blood gasses (9.1%), Carotid doppler (9.1%), Chest X-ray (81.8%), Coagulation studies (9.1%), Creatine kinase (9.1%), Echocardiogram (45.5%), Electrocardiogram (45.5%), Full blood examination (72.7%), Liver function tests (18.2%), Thyroid function tests (9.1%), Serum urea, electrolytes and creatinine (100.0%), Urine microscopy, culture and sensitivities (9.1%)
Osteoporosis	
Mild	Blood glucose level (9.1%), Serum calcium and phosphate (36.4%), Dual energy X-ray absorptiometry (90.9%), Full blood examination (72.7%), Liver function tests (18.2%), Parathyroid hormone (9.1%), Thyroid function tests (18.2%), Serum urea, electrolytes and creatinine (72.7%), Vitamin D (18.2%)
Moderate	Abdominal X-ray (9.1%), Blood glucose level (9.1%), Serum calcium and phosphate (36.4%), Dual energy X-ray absorptiometry (100.0%), Full blood examination (72.7%), Liver function tests (18.2%), Parathyroid hormone (9.1%), Thyroid function tests (9.1%), Serum urea, electrolytes and creatinine (81.8%), Vitamin D (18.2%)
Severe	Blood glucose level (9.1%), Serum calcium and phosphate (36.4%), Chest X-ray (9.1%), Dual energy X-ray absorptiometry (100.0%), Echocardiogram (9.1%), Full blood examination (72.7%), Liver function tests (18.2%), Parathyroid hormone (9.1%), Thyroid function tests (9.1%), Serum urea, electrolytes and creatinine (81.8%), Urine microscopy, culture and sensitivities (9.1%), Vitamin D (18.2%)
Pain	
Mild	Nil
Moderate	Nil
Severe	Full blood examination (9.1%), Serum urea, electrolytes and creatinine (9.1%)
Parkinsonism	
Mild	Serum B12 and folate (9.1%), Computed tomography head (45.5%), Full blood examination (36.4%), Lipid studies (9.1%), Liver function tests (9.1%), Magnetic resonance imaging (head) (9.1%), Serum urea, electrolytes and creatinine (45.5%)
Moderate	Serum B12 and folate (9.1%), Computed tomography head (63.6%), Full blood examination (54.5%), Lipid studies (9.1%), Liver function tests (18.2%), Magnetic resonance imaging (head) (9.1%), Serum urea, electrolytes and creatinine (63.6%), Urine microscopy, culture and sensitivities (9.1%)

CONSEQUENCE SEVERITY LEVEL	INVESTIGATIONS ORDERED DURING RESOLUTION OF HEALTH STATE (% OF EXPERTS SELECTING*)
Severe	Serum B12 and folate (9.1%), Computed tomography head (54.5%), Full blood examination (36.4%), Lipid studies (9.1%), Liver function tests (9.1%), Magnetic resonance imaging (head) (9.1%), Serum urea, electrolytes and creatinine (54.5%), Urine microscopy, culture and sensitivities (9.1%)
Psychosis	
Mild	Serum B12 and folate (9.1%), Computed tomography head (18.2%), Electroencephalogram (9.1%), Full blood examination (63.6%), Iron studies (9.1%), Liver function tests (18.2%), Magnetic resonance imaging (head) (9.1%), Thyroid function tests (27.3%), Serum urea, electrolytes and creatinine (72.7%), Urine microscopy, culture and sensitivities (18.2%)
Moderate	Serum B12 and folate (9.1%), Blood glucose level (9.1%), Computed tomography head (54.5%), Electroencephalogram (9.1%), Full blood examination (81.8%), Iron studies (9.1%), Liver function tests (36.4%), Magnetic resonance imaging (head) (9.1%), Thyroid function tests (45.5%), Serum urea, electrolytes and creatinine (90.9%), Urine microscopy, culture and sensitivities (36.4%)
Severe	Serum B12 and folate (9.1%), Blood cultures (9.1%), Blood glucose level (9.1%), Serum calcium and phosphate (9.1%), Chest X-ray (9.1%), Computed tomography head (63.6%), Electroencephalogram (9.1%), Full blood examination (81.8%), Iron studies (9.1%), Liver function tests (36.4%), Magnetic resonance imaging (head) (9.1%), Thyroid function tests (45.5%), Serum urea, electrolytes and creatinine (90.9%), Urine microscopy, culture and sensitivities (36.4%)
Rash	
Mild	Nil
Moderate	Full blood examination (36.4%), IgE detection (9.1%), Liver function tests (9.1%), Skin biopsy (18.2%), Serum urea, electrolytes and creatinine (36.4%)
Severe	Full blood examination (63.6%), IgE detection (9.1%), Liver function tests (18.2%), Skin biopsy (36.4%), Serum urea, electrolytes and creatinine (72.7%)
Renal Dysfunction	
Mild	Albumin: creatinine ratio (9.1%), Full blood examination (54.5%), Renal ultrasound (9.1%), Serum urea, electrolytes and creatinine (90.9%), Urine microscopy, culture and sensitivities (27.3%)
Moderate	Albumin: creatinine ratio (18.2%), Angiography (9.1%), Blood glucose level (9.1%), Serum calcium and phosphate (18.2%), Full blood examination (63.6%), Liver function tests (9.1%), Parathyroid hormone (9.1%), Renal ultrasound (45.5%), Serum urea, electrolytes and creatinine (90.9%), Urine microscopy, culture and sensitivities (54.5%)
Severe	Albumin: creatinine ratio (18.2%), Arterial blood gasses (9.1%), Blood glucose level (18.2%), Serum calcium and phosphate (27.3%), Chest X-ray (9.1%), Coagulation studies (9.1%), Echocardiogram (9.1%), Full blood examination (72.7%), Iron studies (9.1%), Liver function tests (18.2%), Parathyroid hormone (18.2%), Renal ultrasound (63.6%), Thyroid function tests (9.1%), Serum urea, electrolytes and creatinine (90.9%), Urine microscopy, culture and sensitivities (54.5%)
Respiratory depression	
Mild	Chest X-ray (18.2%), Spirometry (9.1%)
Moderate	Arterial blood gasses (9.1%), Chest X-ray (45.5%), Electrocardiogram (9.1%), Full blood examination (36.4%), Liver function tests (9.1%), Spirometry (81.8%), Serum urea, electrolytes and creatinine (36.4%)
Severe	Arterial blood gasses (54.5%), Blood cultures (9.1%), Serum calcium and phosphate (9.1%), Chest X-ray (54.5%), Computed tomography head (9.1%), Echocardiogram (9.1%), Electrocardiogram (18.2%), Full blood examination (45.5%), Liver function tests (18.2%), Spirometry (63.6%), Thyroid function tests (9.1%), Serum urea, electrolytes and creatinine (45.5%)

CONSEQUENCE SEVERITY LEVEL	INVESTIGATIONS ORDERED DURING RESOLUTION OF HEALTH STATE (% OF EXPERTS SELECTING*)
Seizures	
Mild	Blood glucose level (18.2%), Serum calcium and phosphate (9.1%), Computed tomography head (54.5%), Electrocardiogram (9.1%), Electroencephalogram (45.5%), Full blood examination (54.5%), Liver function tests (9.1%), Magnetic resonance imaging (head) (18.2%), Serum urea, electrolytes and creatinine (72.7%), Urine microscopy, culture and sensitivities (9.1%)
Moderate	Blood glucose level (18.2%), Serum calcium and phosphate (18.2%), Computed tomography head (81.8%), Electrocardiogram (9.1%), Electroencephalogram (63.6%), Full blood examination (81.8%), Liver function tests (27.3%), Magnetic resonance imaging (head) (27.3%), Thyroid function tests (18.2%), Serum urea, electrolytes and creatinine (90.9%), Urine microscopy, culture and sensitivities (9.1%)
Severe	Angiography (9.1%), Blood glucose level (18.2%), Serum calcium and phosphate (18.2%), Computed tomography head (90.9%), Electrocardiogram (9.1%), Electroencephalogram (54.5%), Full blood examination (81.8%), Liver function tests (27.3%), Magnetic resonance imaging (head) (36.4%), Thyroid function tests (18.2%), Serum urea, electrolytes and creatinine (90.9%), Urine microscopy, culture and sensitivities (9.1%)
Serotonin toxicity	
Mild	Full blood examination (18.2%), Serum urea, electrolytes and creatinine (27.3%), Urine microscopy, culture and sensitivities (9.1%)
Moderate	Computed tomography head (18.2%), Creatine kinase (9.1%), Electrocardiogram (18.2%), Full blood examination (45.5%), Liver function tests (18.2%), Serum urea, electrolytes and creatinine (54.5%), Urine microscopy, culture and sensitivities (9.1%)
Severe	Blood cultures (18.2%), Computed tomography head (18.2%), Creatine kinase (18.2%), Echocardiogram (9.1%), Electrocardiogram (36.4%), Full blood examination (54.5%), Liver function tests (27.3%), Thyroid function tests (9.1%), Serum urea, electrolytes and creatinine (63.6%), Urine microscopy, culture and sensitivities (18.2%)
Urinary Incontinence	
Mild	Full blood examination (9.1%), Renal ultrasound (9.1%), Serum urea, electrolytes and creatinine (27.3%), Urine microscopy, culture and sensitivities (54.5%)
Moderate	Abdominal X-ray (9.1%), Blood glucose level (9.1%), Full blood examination (18.2%), Renal ultrasound (36.4%), Serum urea, electrolytes and creatinine (36.4%), Urine microscopy, culture and sensitivities (81.8%)
Severe	Abdominal X-ray (9.1%), Blood glucose level (9.1%), Full blood examination (36.4%), Renal ultrasound (45.5%), Serum urea, electrolytes and creatinine (45.5%), Urine microscopy, culture and sensitivities (81.8%)
Urinary retention	
Mild	Full blood examination (27.3%), Renal ultrasound (36.4%), Serum urea, electrolytes and creatinine (36.4%), Urine microscopy, culture and sensitivities (63.6%)
Moderate	Full blood examination (36.4%), Renal ultrasound (54.5%), Serum urea, electrolytes and creatinine (63.6%), Urine microscopy, culture and sensitivities (90.9%)
Severe	Full blood examination (36.4%), Renal ultrasound (63.6%), Serum urea, electrolytes and creatinine (63.6%), Urine microscopy, culture and sensitivities (81.8%)
Urinary Tract Infection	
Mild	Urine microscopy, culture and sensitivities (54.5%)

CONSEQUENCE SEVERITY LEVEL	INVESTIGATIONS ORDERED DURING RESOLUTION OF HEALTH STATE (% OF EXPERTS SELECTING*)
Moderate	Full blood examination (9.1%), Serum urea, electrolytes and creatinine (9.1%), Urine microscopy, culture and sensitivities (90.9%)
Severe	Blood cultures (18.2%), Full blood examination (45.5%), Renal ultrasound (90.9%), Serum urea, electrolytes and creatinine (63.6%), Urine microscopy, culture and sensitivities (90.9%)

* used to indicate probability of test being ordered

Appendix XVII - Consequences table

TABLE 147 -CONSEQUENCES TABLE - DESCRIPTIVE VIGNETTES AND UTILITIES

CONSEQUENCE	SEVERITY	VIGNETTE	RAW UTILITY (UNADJUSTED FOR DURATION)	
			DISTRIBUTION TYPE	DESCRIPTIVE PARAMETERS*
Acidosis	Mild	Mild signs or symptoms of acidosis which resolve without intervention	Fixed average	1.000
	Moderate	Moderate acidosis requiring medical management without hospitalisation	BetaGeneral	3.563; 0.273; -0.594; 1.000
	Severe	Severe acidosis requiring hospitalisation, electrolyte replacement and/or respiratory support	BetaGeneral	16.150; 3.107; -0.594; 1.000
Alkalosis	Mild	Mild signs or symptoms of alkalosis which resolve without intervention	BetaGeneral	0.992
	Moderate	Moderate alkalosis requiring medical management without hospitalisation	BetaGeneral	1.833; 0.628; -0.594; 1.000
	Severe	Severe alkalosis requiring hospitalisation with electrolyte replacement	BetaGeneral	38.215; 8.054; -0.595; 1.000
Allergic reaction	Mild	Mild allergic reaction not requiring intervention	BetaGeneral	2.681; 0.760; -0.594; 1.000
	Moderate	Moderate allergic reaction requiring topical or oral medications	BetaGeneral	1.000
	Severe	Severe allergic reaction requiring acute medical management	BetaGeneral	6.343; 0.927; -0.594; 1.000
Anaemia	Mild	Mild signs or symptoms of anaemia which resolve without intervention. E.g. haemoglobin of 100-109g/L in pregnant women, 110-119g/L in children and adult women, and 120-129g/L in adult men	Fixed average	16.604; 3.897; -0.595; 1.000
	Moderate	Anaemia requiring medical management and/or modification of medication regimen. E.g. haemoglobin of 70-99g/L in pregnant women, 80-109g/L in children and adult women, and 90-119g/L in adult men	Fixed average	0.729
	Severe	Anaemia requiring hospitalisation and blood product or growth factor support. E.g. haemoglobin of 40-69g/L in pregnant women, 50-79g/L in children and adult women, and 60-89g/L in adult men.	Fixed average	23.259; 7.518; -0.595; 1.000
Anxiety	Mild	Mild signs or symptoms of anxiety which resolve without intervention	BetaGeneral	66.615; 15.578; -0.595; 1.000

Consequence	Severity	Vignette	Raw utility (unadjusted for duration)	
			Distribution type	Descriptive parameters*
	Moderate	Worsening of anxiety requiring modification of existing treatment regimen	BetaGeneral	10.639; 2.752; -0.594; 1.000
	Severe	Anxiety requiring specialist medical attention	Fixed average	0.570
Arrhythmia (incl. tachy- and bradycardia)	Mild	Arrthyhmia that contributes to worsening of other cardiac conditions but not to such an extent as to require medical intervention	BetaGeneral	0.183; 0.053; -0.594; 1.000
	Moderate	Arrthythmia resulting in moderate haemodynamic or myocardial consequences requiring medical attention and treatment	BetaGeneral	167.769; 2.718; -0.594; 1.000
	Severe	Arrthythmia resulting in significant haemodynamic or myocardial complications requiring hospitalisation	BetaGeneral	5.275; 0.137; -0.594; 1.000
Asthma	Mild	Mild asthma which does not require additional intervention	BetaGeneral	0.968
	Moderate	Moderate asthma requiring medical attention and/or modification of medications	BetaGeneral	11.525; 2.768; -0.594; 1.000
	Severe	Severe asthma requiring high level care in a hospital setting	BetaGeneral	18.886; 4.275; -0.595; 1.000
Bleeding, non-specific	Mild	Easy bruising, bleeding from small cuts, petechia, ecchymosis, mild elevation of INR not requiring adjustment of dosage	Fixed average	3.608; 0.127; -0.594; 1.000
	Moderate	Hematoma, epistaxis, blood loss from mouth, vagina, melena, eye bleed, hematuria, hematemesis, moderate elevation of INR requiring modification of dose of anticoagulant	Fixed average	7.467; 0.667; -0.594; 1.000
	Severe	Severe bleeding requiring hospitalisation, blood product and/or haemodynamic support.	Fixed average	1.000
Bone marrow suppression	Mild	Mild signs or symptoms of bone marrow suppression which resolve without intervention	BetaGeneral	1.000
	Moderate	Bone marrow suppression requiring medical management by modification of existing medication regimen	BetaGeneral	6.462; 0.345; -0.594; 1.000
	Severe	Bone marrow suppression requiring hospitalisation and blood product or growth factor support	BetaGeneral	2.357; 0.113; -0.594; 1.000
Cerebrovascular event	Mild	Mild symptoms which resolve (e.g. transient ischemic attack)	BetaGeneral	12.793; 2.525; -0.594; 1.000
	Moderate	Resulting in significant signs and symptoms requiring medical management (e.g. reversible ischaemic neurological deficit)	BetaGeneral	1.000
	Severe	Resulting in severe symptoms and signs requiring hospitalisation and medical management (e.g stroke)	BetaGeneral	7.520; 1.707; -0.594; 1.000
Chronic airways	Mild	Mild chronic airways disease which does not require medical intervention	Fixed average	5.275; 0.137; -0.594; 1.000

CONSEQUENCE	SEVERITY	VIGNETTE	RAW UTILITY (UNADJUSTED FOR DURATION)	
			DISTRIBUTION TYPE	DESCRIPTIVE PARAMETERS*
disease	Moderate	Chronic airways disease requiring medical intervention and/or modification of medication	Fixed average	0.984
	Severe	Severe chronic airways disease requiring hospitalisation and medical intervention	Fixed average	21.654; 3.312; -0.594; 1.000
CNS depression/ sedation	Mild	CNS depression interfering with normal activities, but not requiring medical intervention	BetaGeneral	4.209; 0.512; -0.594; 1.000
	Moderate	CNS depression requiring medical attention and interfering significantly with normal activities	BetaGeneral	56.346; 19.403; -0.595; 1.000
	Severe	Significant CNS depression resulting in loss of consciousness or obtundation	BetaGeneral	48.248; 10.283; -0.595; 1.000
Confusion	Mild	Mild signs or symptoms of confusion which resolve without intervention	BetaGeneral	63.830; 12.952; -0.595; 1.000
	Moderate	Confusion requiring medical management and/or modification of medication regimen	BetaGeneral	1.396; 0.181; -0.594; 1.000
	Severe	Confusion requiring prompt medical management and investigation	BetaGeneral	0.986
Constipation	Mild	Mild signs or symptoms of constipation likely to resolve without intervention	BetaGeneral	48.972; 11.815; -0.595; 1.000
	Moderate	Constipation requiring medical management and/or modification of medication regimen	BetaGeneral	0.235
	Severe	Constipation requiring hospitalisation and medical and/or surgical management	BetaGeneral	0.665
Dementia	Mild	Dementia resulting in some impairment of daily activities only	Fixed average	6.328; 1.942; -0.594; 1.000
	Moderate	Dementia to the extent that independent living is not possible without limited supervision	Fixed average	2.357; 0.113; -0.594; 1.000
	Severe	Dementia to the extent that permanent supervision is required	Fixed average	24.548; 5.106; -0.595; 1.000
Depression	Mild	Mild signs or symptoms of depression which resolve without intervention	BetaGeneral	4.874; 1.737; -0.595; 1.000
	Moderate	Worsening of depression requiring modification of treatment regimen	BetaGeneral	0.685; 0.295; -0.594; 1.000
	Severe	Destabilisation or unmasking of depression requiring specialist medical attention	Fixed average	1.000
Diarrhoea	Mild	Mild signs or symptoms of diarrhoea likely to resolve without intervention	BetaGeneral	0.955
	Moderate	Diarrhoea requiring medical management and/or modification of medication	BetaGeneral	0.984

Consequence	Severity	Vignette	Raw utility (unadjusted for duration)	
			Distribution type	Descriptive parameters*
	Severe	Requiring hospitalisation for significant diarrhoea-related electrolyte and hydration complications	Fixed average	10.805; 2.510; -0.594; 1.000
Gastrointestinal bleeding	Mild	Occult gastrointestinal bleeding likely to require medical management only if persistent	BetaGeneral	4.189; 0.448; -0.594; 1.000
	Moderate	Overt gastrointestinal bleeding requiring medical management	BetaGeneral	76.347; 21.103; -0.595; 1.000
	Severe	Overt gastrointestinal bleeding with haemodynamic consequences requiring prompt medical management	BetaGeneral	0.982
Glaucoma	Mild	Mild elevation of IOP not requiring intervention	Fixed average	1.833; 0.628; -0.594; 1.000
	Moderate	Moderate elevation of IOP requiring medical intervention	Fixed average	8.974; 4.393; -0.595; 1.000
	Severe	Severe glaucoma requiring acute medical or surgical intervention	Fixed average	92.976; 31.452; -0.595; 1.000
Headache	Mild	Mild signs or symptoms of headache which resolve without intervention	BetaGeneral	0.920
	Moderate	Headache requiring oral analgesics and/or modification of medication regimen	BetaGeneral	3.104; 1.341; -0.594; 1.000
	Severe	Severe headache requiring acute medical management and hospitalisation	BetaGeneral	4.440; 2.385; -0.595; 1.000
Heart failure	Mild	Mild signs or symptoms of heart failure (e.g NYHA class II) which resolve without intervention	BetaGeneral	0.729
	Moderate	Resulting in significant signs and symptoms of heart failure (e.g. NYHA class III) requiring medical management by modification of medication regimen	BetaGeneral	5.327; 4.467; -0.595; 1.000
	Severe	Significant signs and symptoms of heart failure (e.g. NYHA class IV) requiring hospitalisation and medical management (e.g. acute pulmonary oedema)	BetaGeneral	13.471; 5.695; -0.595; 1.000
Hypercalcaemia	Mild	Mild signs or symptoms of hypercalacemia which resolve without intervention	BetaGeneral	0.725; 0.275; -0.594; 1.000
	Moderate	Hypercalcaemia requiring medical management and/or modification of medication regimen	BetaGeneral	-0.004
	Severe	Hypercalcaemia requiring prompt medical management and investigation	BetaGeneral	0.109; 0.138; -0.594; 1.000
Hyperglycaemia	Mild	Reduced control of diabetes requiring increased monitoring	BetaGeneral	0.616; 0.031; -0.594; 1.000
	Moderate	Requiring modification of diabetes treatment regimen or significant complications requiring medical management	BetaGeneral	8.454; 2.929; -0.595; 1.000

Consequence	Severity	Vignette	Raw utility (unadjusted for duration)	
			Distribution type	Descriptive parameters*
	Severe	Complications of diabetes requiring specialist medical attention in hospital	BetaGeneral	0.729
Hyperkalaemia	Mild	Mild signs or symptoms of hyperkalaemia which resolve without intervention	Fixed average	80.481; 18.989; -0.595; 1.000
	Moderate	Hyperkalaemia requiring medical management and/or modification of medication regimen	Fixed average	30.035; 16.463; -0.595; 1.000
	Severe	Hyperkalaemia requiring prompt medical management and investigation (e.g. palpitations, bradycardia)	BetaGeneral	6.133; 1.019; -0.594; 1.000
Hypertension	Mild	Mild signs or symptoms of hypertension which resolve without intervention	Fixed average	10.611; 2.230; -0.594; 1.000
	Moderate	Moderate elevation of blood pressure requiring modification of or commencement of medical management	BetaGeneral	1.000
	Severe	Hypertension resulting in acute injury to target organs (e.g. renal, ocular or cerebral) requiring prompt medical management	BetaGeneral	5.275; 0.137; -0.594; 1.000
Hyperthyroidism	Mild	Mild signs or symptoms of hyperthyroidism likely to resolve without intervention	BetaGeneral	1.102; 0.210; -0.594; 1.000
	Moderate	Hyperthyroidism requiring medical management and/or modification of medication regimen	BetaGeneral	4.016; 0.848; -0.594; 1.000
	Severe	Signs or symptoms of hyperthyroidism requiring significant medical management and modification of medication regimen	BetaGeneral	4.963; 1.598; -0.594; 1.000
Hypocalcaemia	Mild	Mild signs or symptoms of hypocalcaemia which resolve without intervention	BetaGeneral	1.336; 0.158; -0.594; 1.000
	Moderate	Hypocalcaemia requiring medical management and/or modification of medication regimen	BetaGeneral	16.732; 3.959; -0.595; 1.000
	Severe	Hypocalcaemia requiring prompt medical management and investigation	BetaGeneral	7.783; 0.642; -0.594; 1.000
Hypoglycaemia	Mild	Mild signs or symptoms of hypoglycaemia which resolve without intervention	BetaGeneral	0.984
	Moderate	Hypoglycaemia requiring additional oral medical management or modification of medication regimen	BetaGeneral	2.826; 1.124; -0.594; 1.000
	Severe	Hypoglycaemia requiring intravenous management	BetaGeneral	3.668; 1.520; -0.594; 1.000
Hypokalaemia	Mild	Mild signs or symptoms of hypokalaemia which resolve without intervention	Fixed average	12.186; 6.002; -0.595; 1.000
	Moderate	Hypokalaemia requiring medical management and/or modification of medication regimen	BetaGeneral	64.897; 21.879; -0.595; 1.000
	Severe	Hypokalaemia requiring prompt medical management and investigation (e.g. palpitations, tacchycardia)	BetaGeneral	10.951; 3.815; -0.595; 1.000

Consequence	Severity	Vignette	Raw utility (unadjusted for duration)	
			Distribution type	Descriptive parameters*
Hypotension	Mild	Clinical symptoms of hypotension not requiring medical intervention	BetaGeneral	66.508; 17.946; -0.595; 1.000
	Moderate	Hypotension requiring medical attention and modification of antihypertensive therapy.	BetaGeneral	0.986
	Severe	Significant haemodynamic consequences of hypotension requiring hospitalisation and intravenous fluid support.	BetaGeneral	3.256; 1.689; -0.595; 1.000
Hypothyroidism	Mild	Mild signs or symptoms of hypothyroidism likely to resolve without intervention	BetaGeneral	-0.259
	Moderate	Hypothyroidism requiring medical management and/or modification of medication regimen	BetaGeneral	-0.132
	Severe	Signs or symptoms of hypothyroidism requiring significant medical management and modification of medication regimen	BetaGeneral	38.387; 9.057; -0.595; 1.000
Infection, general	Mild	Mild signs or symptoms of infection which resolve without intervention	Fixed average	1.336; 0.158; -0.594; 1.000
	Moderate	Infection with moderate complications requiring medical attention and oral antibiotics (e.g. PSI class I pneumonia)	Fixed average	13.470; 5.881; -0.595; 1.000
	Severe	Infection requiring hospitalisation and intravenous antibiotics (eg PSI class III pneumonia)	Fixed average	4.083; 2.497; -0.595; 1.000
Insomnia	Mild	Mild signs or symptoms of insomnia which resolve without intervention	BetaGeneral	1.508; 1.073; -0.595; 1.000
	Moderate	Insomnia requiring medical management	BetaGeneral	0.960
	Severe	Insomnia requiring significant medical intervention and/or modification of medications	BetaGeneral	0.759
Liver disease	Mild	Mild liver disease likely to resolve without intervention	BetaGeneral	0.984
	Moderate	Moderate liver disease requiring modification of medications and medical intervention	BetaGeneral	2.729; 3.292; -0.595; 1.000
	Severe	Severe liver disease requiring hospitalisation and acute medical management	BetaGeneral	3.138; 2.033; -0.595; 1.000
Myocardial ischaemia	Mild	Mild signs or symptoms of angina (e.g. NYHA class I to II) which resolve without intervention	BetaGeneral	0.324; 1.219; -0.595; 1.000
	Moderate	Moderate myocardial ischaemia resulting in significant signs and symptoms requiring medical management by modification of medication regimen (e.g. worsened stable angina)	BetaGeneral	0.729
	Severe	Myocardial ischaemia resulting in severe symptoms and signs requiring hospitalisation and medical management (e.g unstable angina, myocardial infarction)	BetaGeneral	0.107

CONSEQUENCE	SEVERITY	VIGNETTE	RAW UTILITY (UNADJUSTED FOR DURATION)	
			DISTRIBUTION TYPE	DESCRIPTIVE PARAMETERS*
Myopathy	Mild	Mild muscle pain not requiring intervention	BetaGeneral	0.552; 1.770; -0.595; 1.000
	Moderate	Moderate muscle pain requiring modification of medications without elevation in creatine kinase	BetaGeneral	0.373; 2.370; -0.595; 1.000
	Severe	Severe myopathy with elevation of creatine kinase requiring cessation of medication	BetaGeneral	0.570
Nausea and vomiting	Mild	Mild signs or symptoms of nausea likely to resolve without intervention	BetaGeneral	2.053; 1.420; -0.595; 1.000
	Moderate	Nausea requiring medical management and/or modification of medication	BetaGeneral	10.712; 20.745; -0.595; 1.000
	Severe	Requiring hospitalisation for significant vomiting-related electrolyte and hydration complications	BetaGeneral	0.155
Oedema	Mild	Mild signs or symptoms of oedema which resolve without intervention	BetaGeneral	0.390; 2.201; -0.595; 1.000
	Moderate	Moderate oedema resulting in significant symptoms requiring medical management by modification of medication regimen	BetaGeneral	11.619; 16.674; -0.595; 1.000
	Severe	Significant oedema resulting in severe symptoms and signs requiring hospitalisation and management with intravenous diuretics	BetaGeneral	2.201; 2.082; -0.595; 1.000
Osteoporosis	Mild	Worsening of osteoporosis requiring increased monitoring	Fixed average	-0.498
	Moderate	Osteoporosis requiring modification of existing treatment regimen, or commencing treatment for an "at risk" person	Fixed average	-0.267
	Severe	Osteoporosis resulting in hospitalisation due to a major complication (e.g. fracture)	BetaGeneral	0.362
Pain	Mild	Mild pain responding to currently prescribed agents	BetaGeneral	0.647; 2.265; -0.595; 1.000
	Moderate	Moderate pain requiring intensification of oral analgesics	BetaGeneral	0.091
	Severe	Severe pain requiring management using specialist techniques or advice (e.g. hospitalisation, intravenous or epidural opioids or anaesthetics)	BetaGeneral	0.578; 2.586; -0.595; 1.000
Parkinsonism	Mild	Mild Parkinsonian symptoms of tremors and rigidity; slowness, impaired swallowing and speech; disturbance of equilibrium; patient is able to function indepedently	Fixed average	0.645; 4.374; -0.595; 1.000
	Moderate	Swallowing and speech severely impaired; autonomic nervous system disturbances; patients are ADL-dependent, but are able to move without help	Fixed average	3.455; 2.570; -0.595; 1.000

CONSEQUENCE	SEVERITY	VIGNETTE	RAW UTILITY (UNADJUSTED FOR DURATION)	
			DISTRIBUTION TYPE	DESCRIPTIVE PARAMETERS*
	Severe	Severe Parkinsonian symptoms- patient wheelchair and bed-bound; severely handicapped	Fixed average	53.559; 17.422; -0.595; 1.000
Psychosis	Mild	Mild signs or symptoms of psychosis which resolve without intervention	Fixed average	4.630; 2.023; -0.595; 1.000
	Moderate	Worsening of psychotic illness requiring modification of treatment regimen	Fixed average	2.657; 1.531; -0.595; 1.000
	Severe	Destabilisation or unmasking of psychosis requiring specialist medical attention	Fixed average	8.947; 4.296; -0.595; 1.000
Rash	Mild	Localised or mild rash symptoms which respond to "over the counter" treatment	BetaGeneral	1.774; 1.369; -0.595; 1.000
	Moderate	Rash requiring medical attention and topical and/or oral systemic reatment	BetaGeneral	3.972; 5.911; -0.595; 1.000
	Severe	Widespread rash with significant consequences requiring hospitalisation and intravenous systemic treatment	BetaGeneral	0.515; 0.698; -0.595; 1.000
Renal dysfunction	Mild	Mild signs or symptoms of renal dysfunction which resolve without intervention	BetaGeneral	0.667; 2.568; -0.595; 1.000
	Moderate	Renal dysfunction requiring medical management and/or modification of medication regimen	BetaGeneral	7.070; 2.667; -0.595; 1.000
	Severe	Acute decline in renal function requiring prompt medical management and investigation	BetaGeneral	0.984
Respiratory depression	Mild	Mild respiratory depression which will resolve without medical intervention	BetaGeneral	14.439; 6.280; -0.595; 1.000
	Moderate	Requiring medical intervention and/or modification of medications	BetaGeneral	0.539; 0.844; -0.595; 1.000
	Severe	Severe respiratory depression requiring hospitalisation and medical intervention	BetaGeneral	1.432; 5.630; -0.595; 1.000
Seizures	Mild	Mild one-off seizure unlikely to recur or require management	BetaGeneral	0.513; 1.259; -0.595; 1.000
	Moderate	Seizure requiring medical attention or modification of medication regimen	BetaGeneral	0.353; 1.390; -0.595; 1.000
	Severe	Severe seizures requiring hospitalisation and intravenous anticonvulsants	BetaGeneral	6.617; 6.223; -0.595; 1.000
Serotonin toxicity	Mild	Mild signs or symptoms of serotonin toxicity which resolve without intervention	BetaGeneral	0.114; 0.022; -0.594; 1.000
	Moderate	Serotonin toxicity requiring medical management and/or modification of medication regimen	BetaGeneral	0.646; 3.368; -0.595; 1.000
	Severe	Serotonin toxicity requiring prompt medical management and investigation (e.g euphoria, tremor, severe anxiety, palpitations)	BetaGeneral	-0.466

CONSEQUENCE	SEVERITY	VIGNETTE	RAW UTILITY (UNADJUSTED FOR DURATION)	
			DISTRIBUTION TYPE	DESCRIPTIVE PARAMETERS*
Urinary incontinence	Mild	Mild signs or symptoms of urinary incontinence which resolve without intervention	Fixed average	0.158
	Moderate	Urinary incontinence requiring medical management and/or modification of medication regimen	Fixed average	1.651; 2.503; -0.595; 1.000
	Severe	Urinary incontinence requiring hospitalisation and medical and/or surgical management	Fixed average	3.372; 1.653; -0.595; 1.000
Urinary retention	Mild	Symptomatic urinary retention not requiring medical management	Fixed average	6.574; 25.976; -0.595; 1.000
	Moderate	Symptomatic urinary retention requiring medical management	Fixed average	0.657; 2.702; -0.595; 1.000
	Severe	Symptomatic urinary retention requiring catheterisation	Fixed average	0.630; 2.221; -0.595; 1.000
Urinary tract infection	Mild	Mild signs or symptoms of UTI which resolve without intervention	Fixed average	0.750
	Moderate	Moderate UTI requiring medical attention and oral antibiotics	Fixed average	0.750
	Severe	UTI requiring hospitalisation and intravenous antibiotics, e.g. pyelonephritis	Fixed average	0.984

* Parameters: Beta general: (α_1, α_2, minimum, maximum)

TABLE 148 - CONSEQUENCES TABLE - DURATION OF ILL HEALTH AND HOSPITALISATION DATA

		HOSPITALISATION DURATION, COST AND SOURCE				DURATION OF ILL HEALTH	
CONSEQUENCE	SEVERITY	LENGTH OF ADMISSION (DAYS)	COST ($)	AR-DRG CODE (VERSION 5.1, NATIONAL PUBLIC HOSPITALS 2006-2007)	COMMENTS	DISTRIBUTION TYPE	DESCRIPTIVE PARAMETERS*
Acidosis	Mild	0.0	0			Beta	0.015; 0.155
	Moderate	0.0	0			BetaGeneral	1.186; 36.478; 0; 365
	Severe	3.7	3 437.85	K62A, K62B, K62C	Mean of three DRGs weighted for number of occurrences	BetaGeneral	1.242; 19.038; 0; 365
Alkalosis	Mild	0.0	0			Beta	0.022; 0.216
	Moderate	0.0	0			BetaGeneral	0.942; 38.513; 0; 365
	Severe	3.7	3 437.85	K62A, K62B, K62C	Mean of three DRGs weighted for number of occurrences	BetaGeneral	1.620; 31.697; 0; 365
Allergic reaction	Mild	0.0	0			Beta	1.413; 95.116
	Moderate	0.0	0			Beta	1.748; 44.434
	Severe	1.3	1 293.00	X61Z		BetaGeneral	2.115; 89.553; 0; 365
Anaemia	Mild	0.0	0			Beta	0.200; 1.298
	Moderate	0.0	0			Beta	0.678; 2.930
	Severe	1.9	5 311.11	Q61A, Q61B, Q61C		BetaGeneral	1.696; 17.345; 0; 365
Anxiety	Mild	0.0	0			Beta	0.190; 1.016
	Moderate	0.0	0			BetaGeneral	0.621; 5.273; 0; 365
	Severe	4.2	3 766.00	U65Z		BetaGeneral	0.626; 2.286; 0; 365
Arrhythmia (incl.	Mild	0.0	0			BetaGeneral	1.160; 50.865; 0; 365

Consequence	Severity	Hospitalisation duration, cost and source				Duration of ill health	
		Length of admission (days)	Cost ($)	AR-DRG code (version 5.1, National public hospitals 2006-2007)	Comments	Distribution type	Descriptive parameters*
tachy- and bradycardia)	Moderate	0.0	0			BetaGeneral	1.039; 15.886; 0; 365
	Severe	3.0	2 640.48	F70A, F70B, F71A, F71B	Mean of four DRGs weighted for number of occurrences	BetaGeneral	0.945; 6.667; 0; 365
Asthma	Mild	0.0	0			Beta	0.832; 11.423
	Moderate	0.0	0			BetaGeneral	1.539; 38.344; 0; 365
	Severe	3.5	3 194.67	E69A, E69B	Mean of two DRGs weighted for number of occurrences	BetaGeneral	0.926; 7.796; 0; 365
Bleeding, non-specific	Mild	0.0	0			Beta	0.324; 10.231
	Moderate	0.0	0			BetaGeneral	1.662; 78.117; 0; 365
	Severe	3.6	3 393.41	B63Z, B70A, B70B, B70C, B70D, B78A, B78B, E67A, E67B, E73A, E73B, E73C, F42A, F75A, F75B, F75C, G42A, G42B, G45A, G45B, G61A, G61B, G70A, G70B, H63A, H63B, L65A, L65B, L67A, L67B, L67C, Q60A, Q60B, Q60C, Q61A, Q61B, Q61C, S65A, S65B, S65C	Mean of forty DRGs weighted for number of occurrences	BetaGeneral	1.270; 19.487; 0; 365
Bone marrow suppression	Mild	0.0	0			Beta	0.443; 6.569
	Moderate	0.0	0			Beta	0.215; 1.013
	Severe	2.2	2 114.07	Q61A, Q61B, Q61C, Q60A, Q60B, Q60C, Q62Z	Mean of seven DRGs weighted for number of occurrences	BetaGeneral	0.784; 4.117; 0; 365
Cerebrovascular event	Mild	0.0	0			Beta	1.909; 49.010
	Moderate	3.6	3 172.63	B69A, B69B	Mean of two DRGs weighted for number of occurrences	BetaGeneral	2.261; 79.054; 0; 365

		Hospitalisation duration, cost and source				Duration of ill health	
Consequence	**Severity**	**Length of admission (days)**	**Cost ($)**	**AR-DRG code (version 5.1, National public hospitals 2006-2007)**	**Comments**	**Distribution type**	**Descriptive parameters***
	Severe	8.6	7 901.59	B70A, B70B, B70C, B70D	Mean of four DRGs weighted for number of occurrences	Fixed average	146
Chronic airways disease	Mild	0.0	0			Beta	0.608; 6.228
	Moderate	0.0	0			BetaGeneral	1.395; 24.715; 0; 365
	Severe	6.2	4 969.64	E65A, E65B	Mean of two DRGs weighted for number of occurrences	Fixed average	103.357
CNS depression/ sedation	Mild	0.0	0			Beta	0.477; 5.538
	Moderate	0.0	0			BetaGeneral	0.766; 9.107; 0; 365
	Severe	2.0	9 619.77	B80Z, W61Z	Mean of two DRGs weighted for number of occurrences	Fixed average	77.538
Confusion	Mild	0.0	0			Beta	0.837; 16.032
	Moderate	0.0	0			BetaGeneral	1.053; 21.166; 0; 365
	Severe	7.6	5 662.98	B64A, B64B	Mean of two DRGs weighted for number of occurrences	Fixed average	60
Constipation	Mild	0.0	0			Beta	0.251; 3.828
	Moderate	0.0	0			Beta	0.343; 2.585
	Severe	3.8	3 538.17	G65A, G65B	Mean of two DRGs weighted for number of occurrences	BetaGeneral	0.958; 14.560; 0; 365
Dementia	Mild	0.0	0			Fixed average	55
	Moderate	0.0	0			Fixed average	151.714
	Severe	6.4	4 832.71	B67A, B67B, B67C	Mean of three DRGs weighted for number of occurrences	Fixed average	262.154

		Hospitalisation duration, cost and source				Duration of ill health	
Consequence	**Severity**	**Length of admission (days)**	**Cost ($)**	**AR-DRG code (version 5.1, National public hospitals 2006-2007)**	**Comments**	**Distribution type**	**Descriptive parameters***
Depression	Mild	0.0	0			Beta	0.599; 6.165
	Moderate	0.0	0			BetaGeneral	0.986; 10.456; 0; 365
	Severe	12.8	7 932.04	U63A, U63B, U64Z	Mean of three DRGs weighted for number of occurrences	Fixed average	92.692
Diarrhoea	Mild	0.0	0			Beta	1.121; 38.098
	Moderate	0.0	0			BetaGeneral	1.663; 75.604; 0; 365
	Severe	2.1	4 220.00	G43Z, G44A, G44B, G44C, G67B, G68A	Mean of six DRGs weighted for number of occurrences	BetaGeneral	1.539; 37.737; 0; 365
Gastrointestinal bleeding	Mild	0.0	0			Beta	0.771; 40.757
	Moderate	1.6	1 501.00	G61B		BetaGeneral	1.703; 72.464; 0; 365
	Severe	3.3	2 830.00	G61A		BetaGeneral	0.708; 7.352; 0; 365
Glaucoma	Mild	0.0	0			Beta	0.320; 5.495
	Moderate	0.0	0			BetaGeneral	0.523; 6.274; 0; 365
	Severe	1.5	2 976.15	C15A, C15B	Mean of two DRGs weighted for number of occurrences	Fixed average	45.462
Headache	Mild	0.0	0			Beta	0.164; 3.165
	Moderate	0.0	0			Beta	0.708; 7.763
	Severe	1.6	1 566.00	B77Z		BetaGeneral	1.331; 26.677; 0; 365
Heart failure	Mild	0.0	0			Fixed average	33.143
	Moderate	0.0	0			Fixed average	49.357

		Hospitalisation duration, cost and source				Duration of ill health	
Consequence	**Severity**	**Length of admission (days)**	**Cost ($)**	**AR-DRG code (version 5.1, National public hospitals 2006-2007)**	**Comments**	**Distribution type**	**Descriptive parameters***
	Severe	6.6	5 518.11	E64Z, F62A, F62B	Mean of three DRGs weighted for number of occurrences	Fixed average	112.571
Hypercalcaemia	Mild	0.0	0			Beta	0.438; 10.505
	Moderate	0.0	0			BetaGeneral	1.459; 48.447; 0; 365
	Severe	3.7	3 437.85	K62A, K62B, K62C	Mean of three DRGs weighted for number of occurrences	BetaGeneral	1.101; 13.772; 0; 365
Hyperglycaemia	Mild	0.0	0			Beta	0.940; 15.608
	Moderate	0.0	0			BetaGeneral	2.871; 96.106; 0; 365
	Severe	4.8	4 481.62	K60A, K60B	Mean of two DRGs weighted for number of occurrences	BetaGeneral	0.700; 4.953; 0; 365
Hyperkalaemia	Mild	0.0	0			Beta	0.203; 7.276
	Moderate	0.0	0			BetaGeneral	1.388; 62.635; 0; 365
	Severe	3.0	2 640.48	F70A, F70B, F71A, F71B	Mean of four DRGs weighted for number of occurrences	BetaGeneral	1.418; 25.523; 0; 365
Hypertension	Mild	0.0	0			Beta	0.104; 5.483
	Moderate	0.0	0			Beta	0.166; 2.381
	Severe	3.0	2 467.71	F67A, F67B	Mean of two DRGs weighted for number of occurrences	Fixed average	43.357
Hyperthyroidism	Mild	0.0	0			Beta	0.869; 16.275
	Moderate	0.0	0			BetaGeneral	1.503; 42.436; 0; 365
	Severe	2.4	6 406.00	K06Z		BetaGeneral	1.377; 14.117; 0; 365

		Hospitalisation duration, cost and source				Duration of ill health	
Consequence	**Severity**	**Length of admission (days)**	**Cost ($)**	**AR-DRG code (version 5.1, National public hospitals 2006-2007)**	**Comments**	**Distribution type**	**Descriptive parameters***
Hypocalcaemia	Mild	0.0	0			Beta	0.455; 11.796
	Moderate	0.0	0			BetaGeneral	1.402; 53.101; 0; 365
	Severe	3.7	3 437.85	K62A, K62B, K62C	Mean of three DRGs weighted for number of occurrences	BetaGeneral	0.869; 11.370; 0; 365
Hypoglycaemia	Mild	0.0	0			Beta	0.360; 9.154
	Moderate	0.0	0			BetaGeneral	1.275; 56.035; 0; 365
	Severe	5.3	4 023.69	K60A, K60B, K62A, K62B, K62C	Mean of five DRGs weighted for number of occurrences	BetaGeneral	1.217; 29.678; 0; 365
Hypokalaemia	Mild	0.0	0			Beta	0.465; 12.312
	Moderate	0.0	0			BetaGeneral	0.861; 29.187; 0; 365
	Severe	3.0	2 640.48	F70A, F70B, F71A, F71B	Mean of four DRGs weighted for number of occurrences	BetaGeneral	0.767; 8.671; 0; 365
Hypotension	Mild	0.0	0			Beta	0.305; 7.053
	Moderate	0.0	0			BetaGeneral	1.253; 45.027; 0; 365
	Severe	3.4	3 197.70	F73A, F73B, F75A, F75B, F75C	Mean of five DRGs weighted for number of occurrences	BetaGeneral	1.110; 17.829; 0; 365
Hypothyroidism	Mild	0.0	0			Beta	0.391; 4.062
	Moderate	0.0	0			Beta	0.491; 2.847
	Severe	3.1	3 850.86	K64A, K64B	Mean of two DRGs weighted for number of occurrences	BetaGeneral	0.957; 11.680; 0; 365
Infection, general	Mild	0.0	0			Beta	1.004; 31.671

Consequence	Severity	Hospitalisation duration, cost and source				Duration of ill health	
		Length of admission (days)	Cost ($)	AR-DRG code (version 5.1, National public hospitals 2006-2007)	Comments	Distribution type	Descriptive parameters*
	Moderate	0.0	0			BetaGeneral	2.019; 72.149; 0; 365
	Severe	3.7	3 508.95	B72A, B72B, C60A, C60B, C63A, C63B, D40Z, D63A, D63B, D66A, D66B, D67A, D67B, E62A, E62B, E62C, E74A, E74B, E74C, F61Z, F75A, F75B, F75C, G67A, G67B, G68A, G68B, G69Z, G70A, G70B, H63A, H63B, I02A, I02B, I12A, I12B, I12C, I20Z, I30Z, I67A, I67B, J12A, J12B, J12C, J60A, J60B, J64A, J64B, J67A, J67B, K62A, K62B, K64A, K64B, L60A, L60B, L60C, L67A, L67B, L67C, Q60A, Q60B, Q60C, Q61A, R01B, R03B, R61A, R61B, R61C, S65A, S65B, S65C, T60B, T61B, T63B, T64B, U62B, U63B	Mean of 78 DRGs weighted for number of occurrences	BetaGeneral	2.000; 30.301; 0; 365
Insomnia	Mild	0.0	0			Beta	0.309; 3.425
	Moderate	0.0	0			BetaGeneral	0.872; 18.162; 0; 365
	Severe	0.0	0			BetaGeneral	0.987; 11.423; 0; 365
Liver disease	Mild	0.0	0			Beta	0.215; 4.630
	Moderate	0.0	0			Beta	0.579; 3.976
	Severe	4.1	4 058.04	H63A, H62B	Mean of two DRGs weighted for number of occurrences	BetaGeneral	0.707; 4.444; 0; 365
Myocardial ischaemia	Mild	0.0	0			BetaGeneral	1.010; 58.698; 0; 365
	Moderate	1.5	1 464.00	F74Z		BetaGeneral	1.201; 32.196; 0; 365
	Severe	3.4	5 414.61	F41A, F41B, F42A, F42B, F60A, F60B, F60C,		BetaGeneral	0.900; 6.974; 0; 365

Consequence	Severity	Hospitalisation duration, cost and source				Duration of ill health	
		Length of admission (days)	Cost ($)	AR-DRG code (version 5.1, National public hospitals 2006-2007)	Comments	Distribution type	Descriptive parameters*
				F72A, F72B			
Myopathy	Mild	0.0	0			Beta	0.192; 1.920
	Moderate	0.0	0			BetaGeneral	0.839; 22.616; 0; 365
	Severe	0.0	0			BetaGeneral	0.770; 8.030; 0; 365
Nausea and vomiting	Mild	0.0	0			Beta	0.644; 20.574
	Moderate	0.0	0			BetaGeneral	1.709; 96.101; 0; 365
	Severe	3.7	3 437.85	K62A, K62B, K62C	Mean of three DRGs weighted for number of occurrences	BetaGeneral	1.175; 31.520; 0; 365
Oedema	Mild	0.0	0			Beta	0.209; 5.015
	Moderate	0.0	0			BetaGeneral	1.119; 40.376; 0; 365
	Severe	5.7	5 408.00	E64Z		BetaGeneral	0.591; 4.366; 0; 365
Osteoporosis	Mild	0.0	0			Fixed average	28
	Moderate	0.0	0			Fixed average	47.286
	Severe	3.7	3 490.57	I60Z, I61Z, I63Z, I74A, I74B, I74C, I75A, I75B, I75C, I77A, I77B, I78A, I78B	Mean of thirteen DRGs weighted for number of occurrences	Fixed average	84.615
Pain	Mild	0.0	0			Beta	0.342; 4.694
	Moderate	0.0	0			BetaGeneral	1.542; 38.695; 0; 365
	Severe	3.7	7 193.60	B03A, B03B, B07A, B07B	Mean of four DRGs weighted for number of occurrences	Fixed average	80

		Hospitalisation duration, cost and source				Duration of ill health	
Consequence	**Severity**	**Length of admission (days)**	**Cost ($)**	**AR-DRG code (version 5.1, national public hospitals 2006-2007)**	**Comments**	**Distribution type**	**Descriptive parameters***
Parkinsonism	Mild	0.0	0			Fixed average	38.143
	Moderate	0.0	0			Fixed average	83.154
	Severe	6.4	4 832.71	B67A, B67B, B67C	Mean of three DRGs weighted for number of occurrences	Fixed average	213.385
Psychosis	Mild	0.0	0			Beta	0.597; 6.430
	Moderate	0.0	0			BetaGeneral	0.527; 3.019; 0; 365
	Severe	23.8	10 683.33	U61A, U61B, U62A, U62B	Mean of four DRGs weighted for number of occurrences	Fixed average	91.692
Rash	Mild	0.0	0			Beta	0.604; 18.616
	Moderate	0.0	0			BetaGeneral	0.989; 28.952; 0; 365
	Severe	2.5	2 220.69	J67A, J67B, J68A, J68B	Mean of four DRGs weighted for number of occurrences	Fixed average	48.214
Renal dysfunction	Mild	0.0	0			Beta	0.509; 36.982
	Moderate	0.0	0			Beta	2.321; 29.848
	Severe	6.5	6 395.05	L60A, L60B, L60C	Mean of three DRGs weighted for number of occurrences	BetaGeneral	0.574; 3.367; 0; 365
Respiratory depression	Mild	0.0	0			Beta	0.765; 22.035
	Moderate	0.0	0			BetaGeneral	1.887; 56.114; 0; 365
	Severe	3.3	3 568.52	E67A, E67B, E75A, E75B, E75C	Mean of five DRGs weighted for number of occurrences	BetaGeneral	0.628; 3.252; 0; 365
Seizures	Mild	0.0	0			Beta	2.391; 99.027

Consequence	Severity	Hospitalisation duration, cost and source				Duration of ill health	
		Length of admission (days)	Cost ($)	AR-DRG code (version 5.1, National public hospitals 2006-2007)	Comments	Distribution type	Descriptive parameters*
	Moderate	0.0	0			Beta	2.280; 35.720
	Severe	2.6	2 780.51	B76A, B76B	Mean of five DRGs weighted for number of occurrences	BetaGeneral	0.925; 11.064; 0; 365
Serotonin toxicity	Mild	0.0	0			Beta	0.409; 10.609
	Moderate	0.0	0			BetaGeneral	2.067; 78.194; 0; 365
	Severe	0.0	0			BetaGeneral	1.993; 45.719; 0; 365
Urinary incontinence	Mild	0.0	0			Beta	0.295; 5.138
	Moderate	0.0	0			BetaGeneral	0.562; 5.484; 0; 365
	Severe	2.8	2 554.40	L65A, L65B	Mean of two DRGs weighted for number of occurrences	Fixed average	100.615
Urinary retention	Mild	0.0	0			Beta	0.391; 10.333
	Moderate	0.0	0			BetaGeneral	1.460; 65.505; 0; 365
	Severe	2.9	4 159.12	L06A, L06B, L09A, L09B	Mean of four DRGs weighted for number of occurrences	BetaGeneral	0.992; 15.372; 0; 365
Urinary tract infection	Mild	0.0	0			Beta	1.369; 72.343
	Moderate	0.0	0			Beta	6.193; 151.447
	Severe	4.3	3 644.55	L63A, L63B, L63C	Mean of three DRGs weighted for number of occurrences	BetaGeneral	2.587; 79.678; 0; 365

* Parameters: Beta general: (α_1, α_2, minimum, maximum); Beta: (α_1, α_2)

TABLE 149 - CONSEQUENCES TABLE- NUMBER OF GP AND SPECIALIST VISITS, AND COST OF INVESTIGATIONS

CONSEQUENCE	SEVERITY	NUMBER OF GP VISITS		NUMBER OF SPECIALIST VISITS		COST OF INVESTIGATIONS ($)
		DISTRIBUTION TYPE	DESCRIPTIVE PARAMETERS*	DISTRIBUTION TYPE	DESCRIPTIVE PARAMETERS*	
Acidosis	Mild	Poisson	1.786	Fixed average	0	$23.60
	Moderate	Poisson	5	Poisson	1.286	$92.06
	Severe	Negative binomial	2.000; 0.255	Negative binomial	1.000; 0.146	$93.15
Alkalosis	Mild	Geometric	0.286	Binomial	1.000; 0.077	$47.69
	Moderate	Poisson	3.571	Beta	1.079; 85.251	$66.06
	Severe	Negative binomial	2.000; 0.250	Poisson	4	$76.13
Allergic reaction	Mild	Beta	1.018; 72.101	Binomial	1.000; 0.077	
	Moderate	Poisson	2.429	Geometric	0.722	$16.29
	Severe	Negative binomial	2.000; 0.304	Beta	4.934; 207.619	$42.83
Anaemia	Mild	Negative binomial	5.000; 0.673	Negative binomial	10.000; 0.949	$124.37
	Moderate	Poisson	3.929	Beta	3.009; 155.981	$414.59
	Severe	Negative binomial	4.000; 0.378	Negative binomial	12.000; 0.734	$491.73
Anxiety	Mild	Poisson	3	Fixed average	0	$5.80
	Moderate	Poisson	5.357	Beta	0.261; 21.626	$130.10
	Severe	Poisson	8.714	Poisson	4.714	$120.80
Arrhythmia (incl. tachy- and bradycardia)	Mild	Negative binomial	18.000; 0.869	Negative binomial	1.000; 0.650	$114.61
	Moderate	Negative binomial	14.000; 0.731	Poisson	2.5	$249.17
	Severe	Poisson	7.429	Poisson	4.643	$261.76

Consequence	Severity	Number of GP visits		Number of specialist visits		Cost of investigations ($)
		Distribution type	Descriptive parameters*	Distribution type	Descriptive parameters*	
Asthma	Mild	Poisson	1.643	Fixed average	0	$6.89
	Moderate	Binomial	9.000; 0.373	Geometric	0.684	$32.50
	Severe	Negative binomial	10.000; 0.657	Negative binomial	6.000; 0.641	$122.91
Bleeding, non-specific	Mild	Beta	2.354; 113.259	Geometric	0.813	$40.18
	Moderate	Negative binomial	1 050.000; 0.997	Beta	1.194; 64.853	$226.98
	Severe	Negative binomial	3.000; 0.359	Negative binomial	4.000; 0.509	$235.96
Bone marrow suppression	Mild	Poisson	2.643	Negative binomial	10.000; 0.949	$67.45
	Moderate	Binomial	14.000; 0.316	Binomial	17.000; 0.147	$100.66
	Severe	Negative binomial	5.000; 0.446	Negative binomial	19.000; 0.776	$180.22
Cerebrovascular event	Mild	Binomial	10.000; 0.336	Poisson	1.5	$443.04
	Moderate	Negative binomial	41.000; 0.890	Beta	1.264; 43.548	$479.61
	Severe	Negative binomial	2.000; 0.200	Beta	1.665; 26.933	$605.75
Chronic airways disease	Mild	Beta	1.898; 60.633	Binomial	1.000; 0.077	$34.31
	Moderate	Beta	1.883; 36.078	Beta	0.790; 57.914	$93.51
	Severe	Poisson	7.154	Beta	2.373; 46.842	$122.61
CNS depression/ sedation	Mild	Beta	3.188; 143.148	Geometric	0.813	$96.77
	Moderate	Poisson	5	Poisson	1.462	$250.02
	Severe	Negative binomial	3.000; 0.284	Geometric	0.112	$350.81
Confusion	Mild	Poisson	2.071	Geometric	0.765	$138.15

Consequence	Severity	Number of GP visits		Number of specialist visits		Cost of investigations ($)
		Distribution type	Descriptive parameters*	Distribution type	Descriptive parameters*	
	Moderate	Poisson	4.071	Geometric	0.481	$226.80
	Severe	Negative binomial	11.000; 0.653	Beta	1.439; 35.532	$329.19
Constipation	Mild	Poisson	1.143	Fixed average	0	
	Moderate	Negative binomial	8.000; 0.737	Geometric	0.813	$90.63
	Severe	Poisson	4.357	Negative binomial	3.000; 0.583	$337.95
Dementia	Mild	Binomial	21.000; 0.153	Geometric	0.542	$236.42
	Moderate	Negative binomial	10.000; 0.639	Beta	2.724; 131.079	$350.45
	Severe	Geometric	0.097	Negative binomial	56.000; 0.948	$384.78
Depression	Mild	Beta	1.221; 38.090	Geometric	0.813	$47.03
	Moderate	Poisson	5.857	Beta	0.713; 87.560	$166.47
	Severe	Negative binomial	3.000; 0.286	Poisson	5.143	$235.07
Diarrhoea	Mild	Binomial	3.000; 0.333	Fixed average	0	
	Moderate	Binomial	4.000; 0.536	Geometric	0.765	$117.47
	Severe	Poisson	3.5	Beta	1.166; 52.366	$127.65
Gastrointestinal bleeding	Mild	Binomial	4.000; 0.500	Geometric	0.765	$106.50
	Moderate	Binomial	8.000; 0.429	Beta	3.436; 171.463	$355.62
	Severe	Negative binomial	12.000; 0.715	Poisson	3.857	$365.72
Glaucoma	Mild	Binomial	4.000; 0.429	Poisson	1.214	$15.13
	Moderate	Poisson	3.071	Binomial	79.000; 0.034	$23.55
	Severe	Negative binomial	26.000; 0.848	Binomial	36.000; 0.129	$43.10

Consequence	Severity	Number of GP visits		Number of specialist visits		Cost of investigations ($)
		Distribution type	Descriptive parameters*	Distribution type	Descriptive parameters*	
Headache	Mild	Geometric	0.56	Fixed average	0	
	Moderate	Poisson	1.786	Geometric	0.765	$42.71
	Severe	Negative binomial	12.000; 0.774	Negative binomial	7.000; 0.772	$224.58
Heart failure	Mild	Negative binomial	12.000; 0.800	Geometric	0.52	$199.06
	Moderate	Negative binomial	5.000; 0.438	Binomial	607.000; 0.003	$295.64
	Severe	Negative binomial	3.000; 0.252	Negative binomial	5.000; 0.507	$328.25
Hypercalcaemia	Mild	Binomial	18.000; 0.087	Geometric	0.765	$71.61
	Moderate	Poisson	3.357	Negative binomial	3.000; 0.639	$102.75
	Severe	Poisson	5.143	Poisson	4.143	$121.98
Hyperglycaemia	Mild	Beta	2.341; 82.769	Binomial	1.000; 0.077	$71.87
	Moderate	Poisson	4.714	Beta	0.506; 56.698	$152.30
	Severe	Beta	1.357; 20.294	Beta	2.285; 48.907	$117.53
Hyperkalaemia	Mild	Binomial	3.000; 0.524	Binomial	1.000; 0.077	$26.50
	Moderate	Poisson	3.643	Geometric	0.619	$77.34
	Severe	Negative binomial	2.000; 0.211	Poisson	3.071	$110.11
Hypertension	Mild	Binomial	187.000; 0.011	Binomial	1.000; 0.077	$49.36
	Moderate	Negative binomial	8.000; 0.633	Geometric	0.867	$197.68
	Severe	Negative binomial	3.000; 0.273	Poisson	3.786	$266.38
Hyperthyroidism	Mild	Negative binomial	3.000; 0.592	Binomial	1.000; 0.077	$152.51
	Moderate	Poisson	3.857	Poisson	1.571	$164.00

Consequence	Severity	Number of GP visits		Number of specialist visits		Cost of investigations ($)
		Distribution type	Descriptive parameters*	Distribution type	Descriptive parameters*	
	Severe	Poisson	5.286	Poisson	3.357	$166.63
Hypocalcaemia	Mild	Binomial	3.000; 0.571	Binomial	1.000; 0.077	$99.71
	Moderate	Poisson	3.929	Binomial	42.000; 0.037	$135.56
	Severe	Poisson	5.214	Binomial	12.000; 0.304	$162.94
Hypoglycaemia	Mild	Binomial	8.000; 0.205	Fixed average	0	$25.47
	Moderate	Poisson	3.643	Geometric	0.52	$84.43
	Severe	Poisson	5.643	Poisson	3.571	$109.49
Hypokalaemia	Mild	Binomial	2.000; 0.786	Geometric	0.813	$28.69
	Moderate	Binomial	15.000; 0.233	Geometric	0.481	$72.12
	Severe	Poisson	5.286	Binomial	17.000; 0.206	$111.59
Hypotension	Mild	Binomial	3.000; 0.500	Fixed average	0	$46.62
	Moderate	Poisson	3.786	Negative binomial	18.000; 0.979	$92.73
	Severe	Negative binomial	7.000; 0.538	Beta	2.141; 53.874	$195.26
Hypothyroidism	Mild	Poisson	2.286	Fixed average	0	$137.29
	Moderate	Binomial	12.000; 0.333	Geometric	0.565	$188.65
	Severe	Negative binomial	19.000; 0.780	Binomial	7.000; 0.367	$189.54
Infection, general	Mild	Negative binomial	12.000; 0.903	Geometric	0.765	
	Moderate	Poisson	2.714	Geometric	0.765	$76.87
	Severe	Poisson	4.143	Geometric	0.286	$125.05
Insomnia	Mild	Binomial	5.000; 0.171	Fixed average	0	

Consequence	Severity	Number of GP visits		Number of specialist visits		Cost of investigations ($)
		Distribution type	Descriptive parameters*	Distribution type	Descriptive parameters*	
	Moderate	Poisson	2.643	Geometric	0.813	$66.37
	Severe	Negative binomial	19.000; 0.787	Geometric	0.448	$73.35
Liver disease	Mild	Geometric	0.424	Geometric	0.867	$30.45
	Moderate	Binomial	7.000; 0.592	Negative binomial	23.000; 0.923	$101.36
	Severe	Negative binomial	5.000; 0.438	Poisson	4.5	$121.10
Myocardial ischaemia	Mild	Binomial	17.000; 0.139	Geometric	0.565	$141.01
	Moderate	Poisson	4.357	Poisson	2	$415.89
	Severe	Poisson	6.286	Negative binomial	9.000; 0.656	$473.10
Myopathy	Mild	Negative binomial	25.000; 0.951	Binomial	1.000; 0.077	$17.40
	Moderate	Poisson	2.786	Geometric	0.684	$51.91
	Severe	Binomial	8.000; 0.580	Poisson	1.769	$110.36
Nausea and vomiting	Mild	Binomial	2.000; 0.464	Fixed average	0	$1.62
	Moderate	Binomial	4.000; 0.589	Geometric	0.706	$43.21
	Severe	Binomial	9.000; 0.365	Poisson	2.214	$85.68
Oedema	Mild	Binomial	2.000; 0.464	Fixed average	0	$12.95
	Moderate	Poisson	2.929	Geometric	0.813	$186.52
	Severe	Poisson	4.786	Poisson	3	$239.72
Osteoporosis	Mild	Poisson	2.143	Binomial	1.000; 0.077	$161.62
	Moderate	Poisson	4.571	Geometric	0.448	$159.14

Consequence	Severity	Number of GP visits		Number of specialist visits		Cost of investigations ($)
		Distribution type	Descriptive parameters*	Distribution type	Descriptive parameters*	
	Severe	Negative binomial	7.000; 0.554	Poisson	3.643	$184.27
Pain	Mild	Poisson	1.429	Fixed average	0	
	Moderate	Binomial	8.000; 0.438	Geometric	0.765	
	Severe	Negative binomial	6.000; 0.475	Negative binomial	12.000; 0.743	$3.18
Parkinsonism	Mild	Negative binomial	77.000; 0.965	Geometric	0.467	$146.32
	Moderate	Negative binomial	11.000; 0.675	Poisson	2.857	$191.65
	Severe	Poisson	7.769	Negative binomial	22.000; 0.819	$167.55
Psychosis	Mild	Binomial	4.000; 0.536	Negative binomial	2.000; 0.757	$168.17
	Moderate	Negative binomial	15.000; 0.737	Negative binomial	2.000; 0.295	$285.24
	Severe	Negative binomial	4.000; 0.388	Poisson	6.846	$312.20
Rash	Mild	Binomial	2.000; 0.286	Fixed average	0	
	Moderate	Binomial	5.000; 0.500	Geometric	0.565	$25.60
	Severe	Poisson	4.071	Poisson	3.571	$47.15
Renal dysfunction	Mild	Poisson	1.571	Binomial	1.000; 0.077	$42.99
	Moderate	Binomial	10.000; 0.386	Negative binomial	12.000; 0.918	$126.55
	Severe	Poisson	6.071	Negative binomial	14.000; 0.775	$176.23
Respiratory depression	Mild	Binomial	2.000; 0.607	Binomial	1.000; 0.154	$12.77
	Moderate	Poisson	3.571	Negative binomial	2.000; 0.722	$63.20
	Severe	Negative binomial	9.000; 0.627	Negative binomial	2.000; 0.298	$146.64
Seizures	Mild	Poisson	2	Geometric	0.5	$262.51

Consequence	Severity	Number of GP visits		Number of specialist visits		Cost of investigations ($)
		Distribution type	Descriptive parameters*	Distribution type	Descriptive parameters*	
	Moderate	Poisson	4.071	Negative binomial	3.000; 0.592	$416.99
	Severe	Poisson	5.286	Negative binomial	6.000; 0.575	$488.78
Serotonin toxicity	Mild	Binomial	2.000; 0.643	Binomial	1.000; 0.077	$9.86
	Moderate	Poisson	3.643	Negative binomial	1.000; 0.333	$64.24
	Severe	Negative binomial	9.000; 0.667	Negative binomial	5.000; 0.636	$119.60
Urinary incontinence	Mild	Binomial	2.000; 0.429	Binomial	1.000; 0.077	$27.63
	Moderate	Binomial	7.000; 0.459	Poisson	1.071	$70.34
	Severe	Negative binomial	13.000; 0.731	Poisson	3.857	$85.00
Urinary retention	Mild	Binomial	2.000; 0.571	Geometric	0.867	$64.01
	Moderate	Poisson	2.643	Binomial	5.000; 0.257	$95.91
	Severe	Poisson	4.214	Poisson	3.214	$103.95
Urinary tract infection	Mild	Binomial	1.000; 0.571	Fixed average	0	$11.29
	Moderate	Geometric	0.424	Fixed average	0	$22.00
	Severe	Binomial	11.000; 0.234	Negative binomial	4.000; 0.683	$142.77

* Parameters: Beta general: (α_1, α_2, minimum, maximum); Beta: (α_1, α_2); Poisson: (λ); Geometric: (p) ; Binomial/ negative binomial: (n, p)

Appendix XVIII - Quality of life study participant information booklet

VALMER Quality Weights Study
Participation Guide

The VALMER medication review assessment system incorporates a health-related quality of life estimate. This is in the form of a "quality weight". Quality weights rate the quality of life of different health states on a scale from 1.0 (the best health attainable) to 0 (dead). Examples of quality weights for different disease states that have been obtained from previous studies are shown in Table 1.

Disease state	Quality weight
Depression, in remission, sertraline maintenance therapy	0.93
Benign prostatic hypertrophy, continued or worsened symptoms without surgery	0.60
Cataracts, vision impairment, moderate	0.45
Stroke, moderate, cognitive deficit	0.37

Table 1 - Examples of quality weights

Quality weights can be derived via several different methods, and currently there is no standard method for obtaining them. Weights obtained via one method do not always correlate with those derived via a different method. In addition, weights reflecting the disability in one population may be quite different to those in another population. This lack of consistency means that reliable quality weights for the VALMER study cannot be obtained from literature sources.

The aim of this study is therefore to develop a set of quality weights for the common conditions (termed "consequences") experienced by the patients in the VALMER dataset.

There are approximately 50 of these consequences, and each consequence has three levels of severity- MILD, MODERATE and SEVERE. Each level of severity of each consequence is described by a short vignette. Two example consequences are shown in Table 2.

Consequence Severity level	Description
Hypertension	
• **Mild**	Mild signs or symptoms of hypertension which resolve without intervention
• **Moderate**	Moderate elevation of blood pressure requiring modification of or commencement of medical management
• **Severe**	Hypertension resulting in acute injury to target organs (e.g. renal, ocular or cerebral) requiring prompt medical management
Hyperkalaemia	
• **Mild**	Mild signs or symptoms of hyperkalaemia which resolve without intervention
• **Moderate**	Hyperkalaemia requiring medical management and/or modification of medication regimen
• **Severe**	Hyperkalaemia requiring prompt medical management and investigation (e.g. palpitations, bradycardia)

Table 2 - Example consequences

1 | Page

To assess the quality of life of a patient experiencing a consequence, you are asked to give your opinion on how that particular consequence will influence five aspects of health (called domains). These are:

- Mobility;
- Self-care;
- Usual activities;
- Pain/discomfort; and
- Anxiety/depression.

Each domain has three possible levels of disability, such as "no problems", "some problems" and "severe problems". Full descriptions of the levels of disability for each domain are shown in Table 3.

DOMAIN Description of level of disability	Survey terminology
Mobility	
• The patient has no problems in walking around	• No problems
• The patient has some problems in walking around	• Some problems
• The patient is confined to bed	• Confined to bed
Self-care	
• The patient has no problems with self-care	• No problems
• The patient has some problems washing or dressing themself	• Some problems
• The patient is unable to wash or dress themself	• Cannot wash or dress
Usual activities (e.g. work, study, housework, family or leisure activities)	
• The patient has no problems with performing their usual activities	• No problems
• The patient has some problems with performing their usual activities	• Some problems
• The patient is unable to perform their usual activities	• Cannot perform
Pain/discomfort	
• The patient has no pain or discomfort	• None
• The patient has some pain or discomfort	• Some
• The patient has extreme pain or discomfort	• Extreme
Anxiety/depression	
• The patient is not anxious or depressed	• None
• The patient is moderately anxious or depressed	• Moderate
• The patient is extremely anxious or depressed	• Extreme

Table 3 - Descriptions of disability associated with health domains

To participate in this study, you are asked to complete a series of three online questionnaires. Each page of the questionnaires assesses a different consequence at *mild*, *moderate* and *severe* levels of severity. A sample page is shown in Figure 1. To simplify the presentation of domains descriptions, each has been simplified, as shown in the "Survey terminology" column of Table 3.

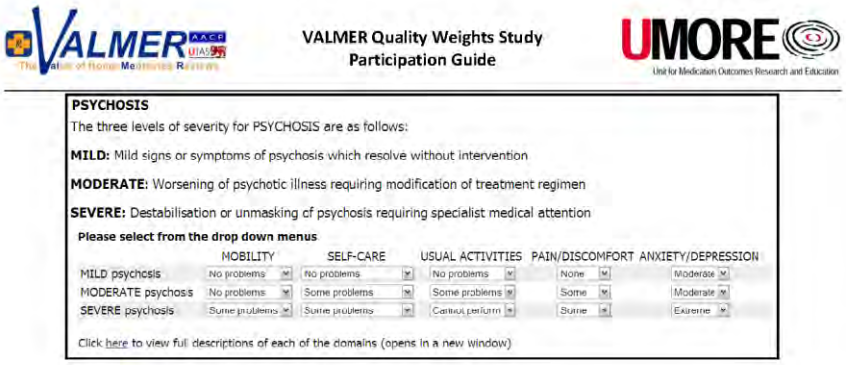


Figure 1 - Example quality weight assessment

In this hypothetical example, the respondent has indicated that a patient with *mild* or *moderate* psychosis has no problems with mobility; whereas a patient with *severe* psychosis has some problems with mobility. You can also see how the respondent has rated the remaining four domains at the three severity levels.

Your responses will be mapped to a standardised value set to derive a quality weight for each consequence at each level of severity.

When rating each consequence, please consider the *acute* state of the condition, rather than chronic complications of it. For example, if you are rating "mild hypertension", your assessment should reflect how a patient feels whilst experiencing only hypertension, rather than long-term sequelae of hypertension such as kidney disease or stroke.

There are 36 consequences to be assessed. These have been arbitrarily split into three groups of 12 so that assessors do not have to complete the study in a single sitting. Each group of 12 consequences should not take any more than 30 minutes to complete. For each group of 12 consequences that is completed, participants are reimbursed $120.

Thanks you for your interest. Please contact Andrew Stafford at the University of Tasmania (andrews5@utas.edu.au or 03 6226 1715) if you require any further information.

To participate in this study, the questionnaires may be accessed at
http://www.pharmacy.utas.edu.au/UMORE/projects/VALMER/qol2.htm

password: Umore

Appendix XIX - Supplementary DRP data tables

TABLE 150 - NUMBER OF DRPS DOCUMENTED BY PHARMACISTS IN HMR REPORTS CLASSED ACCORDING TO THE MEDICAL CONDITIONS ASSOCIATED WITH THEM

	TYPE AND SUBTYPE OF DRP																																		
	DRUG SELECTION							OVER- OR UNDERDOSE			COMPLIANCE AND CONCORDANCE					UNTREATED INDICATIONS			MONITORING			EDUCATION					NON-CLINICAL					TOXICITY				
MEDICAL CONDITION	DUPLICATION	DRUG INTERACTION	WRONG DRUG	WRONG DOSAGE FORM	UNNECESSARY THERAPY/ NO APPARENT CURRENT INDICATION	CONTRAINDICATIONS APPARENT	OTHER DRUG SELECTION PROBLEM	DOSE TOO HIGH	DOSE TOO LOW	OTHER DOSE PROBLEM	TAKING TOO LITTLE	TAKING TOO MUCH	DIFFICULTY USING DOSAGE FORM	PATIENT USING OUT OF DATE MEDICATION	OTHER COMPLIANCE PROBLEM	CONDITION NOT ADEQUATELY TREATED	THERAPY REQUIRED	OTHER UNTREATED INDICATION PROBLEM	LABORATORY MONITORING	NON-LABORATORY MONITORING	OTHER MONITORING PROBLEM	PATIENT DRUG INFORMATION REQUEST	CONFUSION ABOUT THERAPY	DEMONSTRATION OF DEVICE	DISEASE MANAGEMENT OR ADVICE	OTHER EDUCATION OR INFORMATION PROBLEM	WEIGHT MANAGEMENT PROBLEM	DIETARY PROBLEM	SMOKING PROBLEM	ALCOHOL PROBLEM	OTHER NON-CLINICAL PROBLEM	TOXICITY CAUSED BY DOSE	TOXICITY CAUSED BY DRUG INTERACTION	TOXICITY EVIDENT	OTHER TOXICITY/ ADVERSE EFFECT PROBLEM	TOTAL
Diabetes, non-insulin dependent	1	2			4	10	1	4	3	4	5				1	21	27		10	8	1			1	3		2	3				3		7		**121**
General symptom/ complaint, other *					1					2	1	2				75	2		1						1									2		**87**
Hypertension, uncomplicated		1			1	7	2			1	4				2	45	10	1	1	5							1							3		**84**
Lipid disorder	1	2			1		1	2	1	2	1				1	27	16		8													1		4		**68**
Osteoporosis	1					1		4	1	1	1				3	24	17		7															2		**62**
Constipation		1			4	2		3		1	2					13	7															1	2	24		**60**
Urinary disease, other		6				15		19	1							2	2		11								1	2				1				**60**
Oesophagus disease	2	2			8	4		11	2	1	1	1				8	2		1														2		**45**
Osteoarthrosis, other		2				3		3	4	1					1	20	3					1									1				**39**
Sleep disturbance					2	3	1	1	1			1			1	9	2														1		14		**36**
Heart failure	1				1	6	1	2	7		1				1	6	2		2	1							1				1				**33**

	TYPE AND SUBTYPE OF DRP																																						
	DRUG SELECTION							OVER- OR UNDERDOSE			COMPLIANCE AND CONCORDANCE					UNTREATED INDICATIONS			MONITORING			EDUCATION					NON-CLINICAL					TOXICITY								
MEDICAL CONDITION	DUPLICATION	DRUG INTERACTION	WRONG DRUG	WRONG DOSAGE FORM	UNNECESSARY THERAPY/ NO APPARENT CURRENT INDICATION	CONTRAINDICATIONS APPARENT	OTHER DRUG SELECTION PROBLEM	DOSE TOO HIGH	DOSE TOO LOW	OTHER DOSE PROBLEM	TAKING TOO LITTLE	TAKING TOO MUCH	DIFFICULTY USING DOSAGE FORM	PATIENT USING OUT OF DATE MEDICATION	OTHER COMPLIANCE PROBLEM	CONDITION NOT ADEQUATELY TREATED	THERAPY REQUIRED	OTHER UNTREATED INDICATION PROBLEM	LABORATORY MONITORING	NON-LABORATORY MONITORING	OTHER MONITORING PROBLEM	PATIENT DRUG INFORMATION REQUEST	CONFUSION ABOUT THERAPY	DEMONSTRATION OF DEVICE	DISEASE MANAGEMENT OR ADVICE	OTHER EDUCATION OR INFORMATION PROBLEM	WEIGHT MANAGEMENT PROBLEM	DIETARY PROBLEM	SMOKING PROBLEM	ALCOHOL PROBLEM	OTHER NON-CLINICAL PROBLEM	TOXICITY CAUSED BY DOSE	TOXICITY CAUSED BY DRUG INTERACTION	TOXICITY EVIDENT	OTHER TOXICITY/ ADVERSE EFFECT PROBLEM	TOTAL
Trauma/ injury not otherwise specified		1			2	3										1	8		6	1										1	1			9		**33**
Vitamin/ nutritional deficiency								1	5		1						8		14															3		**32**
Chronic obstructive pulmonary disease				1	1	2		1			4		3			12			1					1	3	1										**30**
Shortness of breath/ dyspnoea				1	2	1					3		2			7	6						1					1						6		**30**
Vertigo/ dizziness		2			1	2		1									1															3	4	16		**30**
Asthma	1				1	5		2		1	7	2				4	1	1					2	1										1		**29**
Abnormal result investigation not otherwise specified		9			2	1													3									1					2	10		**28**
Cough	1										1		1			2	1																	17		**23**
Mouth/ tongue/ lip symptom/ complaint		1			1	1										1	1																2	15		**22**
Depressive disorder					4	1		1		1	2					6	2		2	1															1		**21**
Gout	1	1			4			6	1		1	1				2																1			1		**19**
Leg/ thigh symptom/ complaint					1	3			1		1					3	1															1	1	7		**19**
Diarrhoea																1	3										1					6	1	6		**18**
Nausea					1												1		1													4		11		**18**

	TYPE AND SUBTYPE OF DRP																																		
	DRUG SELECTION							OVER- OR UNDERDOSE			COMPLIANCE AND CONCORDANCE					UNTREATED INDICATIONS			MONITORING			EDUCATION					NON-CLINICAL					TOXICITY				
MEDICAL CONDITION	DUPLICATION	DRUG INTERACTION	WRONG DRUG	WRONG DOSAGE FORM	UNNECESSARY THERAPY/ NO APPARENT CURRENT INDICATION	CONTRAINDICATIONS APPARENT	OTHER DRUG SELECTION PROBLEM	DOSE TOO HIGH	DOSE TOO LOW	OTHER DOSE PROBLEM	TAKING TOO LITTLE	TAKING TOO MUCH	DIFFICULTY USING DOSAGE FORM	PATIENT USING OUT OF DATE MEDICATION	OTHER COMPLIANCE PROBLEM	CONDITION NOT ADEQUATELY TREATED	THERAPY REQUIRED	OTHER UNTREATED INDICATION PROBLEM	LABORATORY MONITORING	NON-LABORATORY MONITORING	OTHER MONITORING PROBLEM	PATIENT DRUG INFORMATION REQUEST	CONFUSION ABOUT THERAPY	DEMONSTRATION OF DEVICE	DISEASE MANAGEMENT OR ADVICE	OTHER EDUCATION OR INFORMATION PROBLEM	WEIGHT MANAGEMENT PROBLEM	DIETARY PROBLEM	SMOKING PROBLEM	ALCOHOL PROBLEM	OTHER NON-CLINICAL PROBLEM	TOXICITY CAUSED BY DOSE	TOXICITY CAUSED BY DRUG INTERACTION	TOXICITY EVIDENT	OTHER TOXICITY/ ADVERSE EFFECT PROBLEM	TOTAL
Muscle symptom/ complaint not otherwise specified						3			1							1	2		2													1	1	6		**17**
Atrial fibrillation/ flutter		2			1						1		1			2	5																	3		**15**
Cystitis/ urinary infection, other			1			4	1		1		1						5																	2		**15**
Ischaemic heart disease with angina	1									1	4					6	2												1							**15**
Tobacco abuse									1							2	1												11							**15**
Urinary frequency/ urgency					1	1				1						1	1															1	1	1	7		**15**
Back symptom/ complaint					1											12	1																			**14**
Swollen ankles/ oedema								1			1						1															1		10		**14**
Weakness/ tiredness general		1				1				1						1	3		1													1		5		**14**
Incontinence urine					2												3	1																6		**12**
Pruritus																																	1	10		**11**
Swallowing problems													8				2														1					**11**
Blood symptom/ complaint											1																						3	6		**10**
Cardiovascular symptom/								1									1											1				1		6		**10**

	TYPE AND SUBTYPE OF DRP																																				
	DRUG SELECTION							OVER- OR UNDERDOSE			COMPLIANCE AND CONCORDANCE					UNTREATED INDICATIONS			MONITORING			EDUCATION					NON-CLINICAL					TOXICITY				
MEDICAL CONDITION	DUPLICATION	DRUG INTERACTION	WRONG DRUG	WRONG DOSAGE FORM	UNNECESSARY THERAPY/ NO APPARENT CURRENT INDICATION	CONTRAINDICATIONS APPARENT	OTHER DRUG SELECTION PROBLEM	DOSE TOO HIGH	DOSE TOO LOW	OTHER DOSE PROBLEM	TAKING TOO LITTLE	TAKING TOO MUCH	DIFFICULTY USING DOSAGE FORM	PATIENT USING OUT OF DATE MEDICATION	OTHER COMPLIANCE PROBLEM	CONDITION NOT ADEQUATELY TREATED	THERAPY REQUIRED	OTHER UNTREATED INDICATION PROBLEM	LABORATORY MONITORING	NON-LABORATORY MONITORING	OTHER MONITORING PROBLEM	PATIENT DRUG INFORMATION REQUEST	CONFUSION ABOUT THERAPY	DEMONSTRATION OF DEVICE	DISEASE MANAGEMENT OR ADVICE	OTHER EDUCATION OR INFORMATION PROBLEM	WEIGHT MANAGEMENT PROBLEM	DIETARY PROBLEM	SMOKING PROBLEM	ALCOHOL PROBLEM	OTHER NON-CLINICAL PROBLEM	TOXICITY CAUSED BY DOSE	TOXICITY CAUSED BY DRUG INTERACTION	TOXICITY EVIDENT	OTHER TOXICITY/ ADVERSE EFFECT PROBLEM	TOTAL
complaint, other																																					
Pain, muscle																			1													1		8		**10**
Ischaemic heart disease without angina					1						1		1	1		4	1																			**9**
Memory disturbance					1	2											1																	5		**9**
Feeling anxious/ nervous/ tense					1	2		1					1			1	1		1																	**8**
Glaucoma						1					4					1	2																			**8**
Headache						1		1								1	1																	4		**8**
Knee symptom/ complaint		1														5	1								1											**8**
Parkinsonism		1				2				1	1				1				1															1		**8**
Acute myocardial infarction						1										4	2																			**7**
Heartburn								1								3																		3		**7**
Obesity																	1	1									5									**7**
Peptic ulcer, other		1				1		1									1																	2	1	**7**
Rheumatoid/ seropositive arthritis	1										1					2	1							1								1				**7**
Sneezing/ nasal congestion											2					1	1																	3		**7**
Dyspepsia/																2														1				3		**6**

	TYPE AND SUBTYPE OF DRP																																		
	DRUG SELECTION							OVER- OR UNDERDOSE			COMPLIANCE AND CONCORDANCE					UNTREATED INDICATIONS			MONITORING			EDUCATION					NON-CLINICAL					TOXICITY				
MEDICAL CONDITION	DUPLICATION	DRUG INTERACTION	WRONG DRUG	WRONG DOSAGE FORM	UNNECESSARY THERAPY/ NO APPARENT CURRENT INDICATION	CONTRAINDICATIONS APPARENT	OTHER DRUG SELECTION PROBLEM	DOSE TOO HIGH	DOSE TOO LOW	OTHER DOSE PROBLEM	TAKING TOO LITTLE	TAKING TOO MUCH	DIFFICULTY USING DOSAGE FORM	PATIENT USING OUT OF DATE MEDICATION	OTHER COMPLIANCE PROBLEM	CONDITION NOT ADEQUATELY TREATED	THERAPY REQUIRED	OTHER UNTREATED INDICATION PROBLEM	LABORATORY MONITORING	NON-LABORATORY MONITORING	OTHER MONITORING PROBLEM	PATIENT DRUG INFORMATION REQUEST	CONFUSION ABOUT THERAPY	DEMONSTRATION OF DEVICE	DISEASE MANAGEMENT OR ADVICE	OTHER EDUCATION OR INFORMATION PROBLEM	WEIGHT MANAGEMENT PROBLEM	DIETARY PROBLEM	SMOKING PROBLEM	ALCOHOL PROBLEM	OTHER NON-CLINICAL PROBLEM	TOXICITY CAUSED BY DOSE	TOXICITY CAUSED BY DRUG INTERACTION	TOXICITY EVIDENT	OTHER TOXICITY/ ADVERSE EFFECT PROBLEM	TOTAL
indigestion																																			
Hypothyroidism/ myxoedema	1	2										1							2																**6**
Musculoskeletal disease, other		3															1		2																**6**
Anaemia other/ unspecified					1												1		1														2		**5**
Dermatitis, contact/ allergic											1					1	1								1								1		**5**
Loss of appetite					1																							1				1	2		**5**
Postural hypotension																																1	2	2	**5**
Restless legs						1										1	1		1															1	**5**
Stroke/ cerebrovascular accident	1					1											2														1				**5**
Abnormal urine test not otherwise specified																2	2																		**4**
Flatulence/ gas/ belching																	2																2		**4**
Fracture: other					1											1	2																		**4**
Hip symptom/ complaint																3	1																		**4**
Neurological symptom/																	3		1																**4**

	TYPE AND SUBTYPE OF DRP																																				
	DRUG SELECTION							OVER- OR UNDERDOSE			COMPLIANCE AND CONCORDANCE					UNTREATED INDICATIONS			MONITORING			EDUCATION					NON-CLINICAL					TOXICITY				
MEDICAL CONDITION	DUPLICATION	DRUG INTERACTION	WRONG DRUG	WRONG DOSAGE FORM	UNNECESSARY THERAPY/ NO APPARENT CURRENT INDICATION	CONTRAINDICATIONS APPARENT	OTHER DRUG SELECTION PROBLEM	DOSE TOO HIGH	DOSE TOO LOW	OTHER DOSE PROBLEM	TAKING TOO LITTLE	TAKING TOO MUCH	DIFFICULTY USING DOSAGE FORM	PATIENT USING OUT OF DATE MEDICATION	OTHER COMPLIANCE PROBLEM	CONDITION NOT ADEQUATELY TREATED	THERAPY REQUIRED	OTHER UNTREATED INDICATION PROBLEM	LABORATORY MONITORING	NON-LABORATORY MONITORING	OTHER MONITORING PROBLEM	PATIENT DRUG INFORMATION REQUEST	CONFUSION ABOUT THERAPY	DEMONSTRATION OF DEVICE	DISEASE MANAGEMENT OR ADVICE	OTHER EDUCATION OR INFORMATION PROBLEM	WEIGHT MANAGEMENT PROBLEM	DIETARY PROBLEM	SMOKING PROBLEM	ALCOHOL PROBLEM	OTHER NON-CLINICAL PROBLEM	TOXICITY CAUSED BY DOSE	TOXICITY CAUSED BY DRUG INTERACTION	TOXICITY EVIDENT	OTHER TOXICITY/ ADVERSE EFFECT PROBLEM	TOTAL
complaint, other																																					
Pain, chest not otherwise specified															1		2		1																		**4**
Sensation disturbance, other																																	1	3		**4**
Wheezing											1					1	1																1			**4**
Abnormal involuntary movements																	1																	2		**3**
Benign prostatic hypertrophy					1											1				1																**3**
Cardiac arrhythmia not otherwise specified		1																														1	1			**3**
Diverticular disease																	2																	1		**3**
Eye/ adnexa disease, other						1										1																		1		**3**
Pain, abdominal epigastric																1																		2		**3**
Pain/ cramps, abdominal general						1																										1		1		**3**
Rectal bleeding																																		3		**3**
Skin disease, other		1															1																	1		**3**
Skin texture symptom/ complaint																2	1																			**3**

	TYPE AND SUBTYPE OF DRP																																		
	DRUG SELECTION							OVER- OR UNDERDOSE			COMPLIANCE AND CONCORDANCE					UNTREATED INDICATIONS			MONITORING			EDUCATION					NON-CLINICAL					TOXICITY				
MEDICAL CONDITION	DUPLICATION	DRUG INTERACTION	WRONG DRUG	WRONG DOSAGE FORM	UNNECESSARY THERAPY/ NO APPARENT CURRENT INDICATION	CONTRAINDICATIONS APPARENT	OTHER DRUG SELECTION PROBLEM	DOSE TOO HIGH	DOSE TOO LOW	OTHER DOSE PROBLEM	TAKING TOO LITTLE	TAKING TOO MUCH	DIFFICULTY USING DOSAGE FORM	PATIENT USING OUT OF DATE MEDICATION	OTHER COMPLIANCE PROBLEM	CONDITION NOT ADEQUATELY TREATED	THERAPY REQUIRED	OTHER UNTREATED INDICATION PROBLEM	LABORATORY MONITORING	NON-LABORATORY MONITORING	OTHER MONITORING PROBLEM	PATIENT DRUG INFORMATION REQUEST	CONFUSION ABOUT THERAPY	DEMONSTRATION OF DEVICE	DISEASE MANAGEMENT OR ADVICE	OTHER EDUCATION OR INFORMATION PROBLEM	WEIGHT MANAGEMENT PROBLEM	DIETARY PROBLEM	SMOKING PROBLEM	ALCOHOL PROBLEM	OTHER NON-CLINICAL PROBLEM	TOXICITY CAUSED BY DOSE	TOXICITY CAUSED BY DRUG INTERACTION	TOXICITY EVIDENT	OTHER TOXICITY/ ADVERSE EFFECT PROBLEM	TOTAL
Tingling fingers/ feet/ toes																1																	2		**3**
Visual disturbance, other													1																				1	1	**3**
Weight loss																											1					1		1	**3**
Back syndrome with radiating pain																1	1																		**2**
Bleeding, haemorrhage not otherwise specified						1																											1		**2**
Cardiovascular disease, other																	1																	1	**2**
Chronic ulcer skin																	1																	1	**2**
Compliance/ being ill problem											2																								**2**
Dementia						1										1																			**2**
Endocrine/ metabolic/ nutritional disease, other																				1														1	**2**
Fainting/ syncope																	1															1			**2**
Irritable bowel syndrome																	1																1		**2**
Migraine																2																			**2**
Nose bleed/ epistaxis																																	1	1	**2**

	TYPE AND SUBTYPE OF DRP																																		
	DRUG SELECTION							OVER- OR UNDERDOSE			COMPLIANCE AND CONCORDANCE					UNTREATED INDICATIONS			MONITORING			EDUCATION					NON-CLINICAL					TOXICITY				
MEDICAL CONDITION	DUPLICATION	DRUG INTERACTION	WRONG DRUG	WRONG DOSAGE FORM	UNNECESSARY THERAPY/ NO APPARENT CURRENT INDICATION	CONTRAINDICATIONS APPARENT	OTHER DRUG SELECTION PROBLEM	DOSE TOO HIGH	DOSE TOO LOW	OTHER DOSE PROBLEM	TAKING TOO LITTLE	TAKING TOO MUCH	DIFFICULTY USING DOSAGE FORM	PATIENT USING OUT OF DATE MEDICATION	OTHER COMPLIANCE PROBLEM	CONDITION NOT ADEQUATELY TREATED	THERAPY REQUIRED	OTHER UNTREATED INDICATION PROBLEM	LABORATORY MONITORING	NON-LABORATORY MONITORING	OTHER MONITORING PROBLEM	PATIENT DRUG INFORMATION REQUEST	CONFUSION ABOUT THERAPY	DEMONSTRATION OF DEVICE	DISEASE MANAGEMENT OR ADVICE	OTHER EDUCATION OR INFORMATION PROBLEM	WEIGHT MANAGEMENT PROBLEM	DIETARY PROBLEM	SMOKING PROBLEM	ALCOHOL PROBLEM	OTHER NON-CLINICAL PROBLEM	TOXICITY CAUSED BY DOSE	TOXICITY CAUSED BY DRUG INTERACTION	TOXICITY EVIDENT	OTHER TOXICITY/ ADVERSE EFFECT PROBLEM	TOTAL
Overweight																											1						1			**2**
Palpitations/ awareness of heart																																	2			**2**
Phlebitis/ thrombophlebitis		1															1																			**2**
Pulmonary embolism					1			1																												**2**
Shoulder symptom/ complaint																1																		1		**2**
Skin symptom/ complaint, other																																		2		**2**
Sweating problems																																	1	1		**2**
Throat symptom/ complaint																1																		1		**2**
Urination problems, other												1																						1		**2**
Vaginal symptom/ complaint, other						1																									1					**2**
Acute stress reaction																	1																			**1**
Affective psychosis										1																										**1**
Anaemia, vitamin B12/ folate deficiency																			1																	**1**
Atherosclerosis/ peripheral vascular																																		1		**1**

	TYPE AND SUBTYPE OF DRP																																		
	DRUG SELECTION							OVER- OR UNDERDOSE			COMPLIANCE AND CONCORDANCE					UNTREATED INDICATIONS			MONITORING			EDUCATION					NON-CLINICAL					TOXICITY				
MEDICAL CONDITION	DUPLICATION	DRUG INTERACTION	WRONG DRUG	WRONG DOSAGE FORM	UNNECESSARY THERAPY/ NO APPARENT CURRENT INDICATION	CONTRAINDICATIONS APPARENT	OTHER DRUG SELECTION PROBLEM	DOSE TOO HIGH	DOSE TOO LOW	OTHER DOSE PROBLEM	TAKING TOO LITTLE	TAKING TOO MUCH	DIFFICULTY USING DOSAGE FORM	PATIENT USING OUT OF DATE MEDICATION	OTHER COMPLIANCE PROBLEM	CONDITION NOT ADEQUATELY TREATED	THERAPY REQUIRED	OTHER UNTREATED INDICATION PROBLEM	LABORATORY MONITORING	NON-LABORATORY MONITORING	OTHER MONITORING PROBLEM	PATIENT DRUG INFORMATION REQUEST	CONFUSION ABOUT THERAPY	DEMONSTRATION OF DEVICE	DISEASE MANAGEMENT OR ADVICE	OTHER EDUCATION OR INFORMATION PROBLEM	WEIGHT MANAGEMENT PROBLEM	DIETARY PROBLEM	SMOKING PROBLEM	ALCOHOL PROBLEM	OTHER NON-CLINICAL PROBLEM	TOXICITY CAUSED BY DOSE	TOXICITY CAUSED BY DRUG INTERACTION	TOXICITY EVIDENT	OTHER TOXICITY/ ADVERSE EFFECT PROBLEM	TOTAL
disease																																			
Bruise/ contusion																																	I		I
Cerebrovascular disease																	I																		I
Chills																I																			I
Chronic alcohol abuse																	I																		I
Chronic enteritis/ ulcerative colitis						I																													I
Congenital anomaly urinary tract																I																			I
Diabetes, insulin dependent																I																			I
Disturbance of smell/ taste																																	I		I
Duodenal ulcer																																	I		I
Epilepsy										I																									I
Eye discharge																	I																		I
Eye symptom/ complaint, other						I																													I
Fear of musculoskeletal disease, other																			I																I
Hair loss/ baldness																																	I		I
Heart valve disease																			I																I

	TYPE AND SUBTYPE OF DRP																																			
	DRUG SELECTION							OVER- OR UNDERDOSE			COMPLIANCE AND CONCORDANCE					UNTREATED INDICATIONS			MONITORING			EDUCATION					NON-CLINICAL					TOXICITY				
MEDICAL CONDITION	DUPLICATION	DRUG INTERACTION	WRONG DRUG	WRONG DOSAGE FORM	UNNECESSARY THERAPY/ NO APPARENT CURRENT INDICATION	CONTRAINDICATIONS APPARENT	OTHER DRUG SELECTION PROBLEM	DOSE TOO HIGH	DOSE TOO LOW	OTHER DOSE PROBLEM	TAKING TOO LITTLE	TAKING TOO MUCH	DIFFICULTY USING DOSAGE FORM	PATIENT USING OUT OF DATE MEDICATION	OTHER COMPLIANCE PROBLEM	CONDITION NOT ADEQUATELY TREATED	THERAPY REQUIRED	OTHER UNTREATED INDICATION PROBLEM	LABORATORY MONITORING	NON-LABORATORY MONITORING	OTHER MONITORING PROBLEM	PATIENT DRUG INFORMATION REQUEST	CONFUSION ABOUT THERAPY	DEMONSTRATION OF DEVICE	DISEASE MANAGEMENT OR ADVICE	OTHER EDUCATION OR INFORMATION PROBLEM	WEIGHT MANAGEMENT PROBLEM	DIETARY PROBLEM	SMOKING PROBLEM	ALCOHOL PROBLEM	OTHER NON-CLINICAL PROBLEM	TOXICITY CAUSED BY DOSE	TOXICITY CAUSED BY DRUG INTERACTION	TOXICITY EVIDENT	OTHER TOXICITY/ ADVERSE EFFECT PROBLEM	TOTAL
not otherwise specified																																				
Joint symptom/ complaint not otherwise specified																	1																			1
Limited function/ disability eye																																		1		1
Limited function/ disability not otherwise specified																															1					1
Limited function/ disability urinary																										1										1
Liver disease not otherwise specified								1																												1
Malignant neoplasm blood, other																			1																	1
Malignant neoplasm of skin																																		1		1
Melaena																																		1		1
Menopausal symptom/ complaint						1																														1
Mouth/ tongue/ lip disease									1																											1
Neck syndrome																1																				1
Nose symptom/																	1																			1

	TYPE AND SUBTYPE OF DRP																																				
	DRUG SELECTION								OVER- OR UNDERDOSE			COMPLIANCE AND CONCORDANCE					UNTREATED INDICATIONS			MONITORING			EDUCATION					NON-CLINICAL					TOXICITY				
MEDICAL CONDITION	DUPLICATION	DRUG INTERACTION	WRONG DRUG	WRONG DOSAGE FORM	UNNECESSARY THERAPY/ NO APPARENT CURRENT INDICATION	CONTRAINDICATIONS APPARENT	OTHER DRUG SELECTION PROBLEM	DOSE TOO HIGH	DOSE TOO LOW	OTHER DOSE PROBLEM	TAKING TOO LITTLE	TAKING TOO MUCH	DIFFICULTY USING DOSAGE FORM	PATIENT USING OUT OF DATE MEDICATION	OTHER COMPLIANCE PROBLEM	CONDITION NOT ADEQUATELY TREATED	THERAPY REQUIRED	OTHER UNTREATED INDICATION PROBLEM	LABORATORY MONITORING	NON-LABORATORY MONITORING	OTHER MONITORING PROBLEM	PATIENT DRUG INFORMATION REQUEST	CONFUSION ABOUT THERAPY	DEMONSTRATION OF DEVICE	DISEASE MANAGEMENT OR ADVICE	OTHER EDUCATION OR INFORMATION PROBLEM	WEIGHT MANAGEMENT PROBLEM	DIETARY PROBLEM	SMOKING PROBLEM	ALCOHOL PROBLEM	OTHER NON-CLINICAL PROBLEM	TOXICITY CAUSED BY DOSE	TOXICITY CAUSED BY DRUG INTERACTION	TOXICITY EVIDENT	OTHER TOXICITY/ ADVERSE EFFECT PROBLEM	TOTAL
complaint, other																																					
Peripheral neuritis/ neuropathy																1																				1
Pressure/ tightness of heart																1																				1
Psoriasis																1																				1
Red eye																																		1		1
Respiratory disease, other																																		1		1
Respiratory symptom/ complaint, other																1																				1
Sinusitis acute/ chronic											1																									1
Skin infection, other					1																															1
Teeth/ gum symptom/ complaint																																		1		1
Tinnitus, ringing/ buzzing ear								1																												1
Transient cerebral ischaemia																1																				1
Unexplained abnormal white cells		1																																		1

	Type and subtype of DRP																																				
	Drug selection								Over- or underdose			Compliance and concordance					Untreated indications			Monitoring			Education						Non-clinical					Toxicity					
Medical condition	Duplication	Drug interaction	Wrong drug	Wrong dosage form	Unnecessary therapy/ no apparent current indication	Contraindications apparent	Other drug selection problem	Dose too high	Dose too low	Other dose problem	Taking too little	Taking too much	Difficulty using dosage form	Patient using out of date medication	Other compliance problem	Condition not adequately treated	Therapy required	Other untreated indication problem	Laboratory monitoring	Non-laboratory monitoring	Other monitoring problem	Patient drug information request	Confusion about therapy	Demonstration of device	Disease management or advice	Other education or information problem	Weight management problem	Dietary problem	Smoking problem	Alcohol problem	Other non-clinical problem	Toxicity caused by dose	Toxicity caused by drug interaction	Toxicity evident	Other toxicity/ adverse effect problem	Total
Urinary calculus																			1																		1
Vertiginous syndrome																																	1				1
Viral hepatitis																	1																				1
Vomiting																															1						1
Vulval symptom/ complaint																1																					1
Subtype total	**36**	**189**	**1**	**3**	**132**	**135**	**15**	**117**	**45**	**36**	**133**	**13**	**40**	**16**	**119**	**373**	**262**	**3**	**216**	**19**	**3**	**6**	**9**	**9**	**15**	**5**	**11**	**13**	**13**	**4**	**14**	**27**	**39**	**247**	**5**	**2323**

* most frequently *Pain*

TABLE 151 -ATC LEVEL III DRUG GROUPS ASSOCIATED WITH DRP SUBTYPES

	DRP TYPE AND SUBTYPE																																
	DRUG SELECTION							OVER- AND UNDER-DOSE			COMPLIANCE AND CONCORDANCE					UNTREATED INDICATIONS		MONITORING			EDUCATION					NON-CLINICAL				TOXICITY				
DRUG GROUP (ATC LEVEL III)	DUPLICATION	DRUG INTERACTION	WRONG DRUG	WRONG DOSAGE FORM	UNNECESSARY THERAPY/NO APPARENT CURRENT INDICATION	CONTRAINDICATIONS APPARENT	OTHER DRUG SELECTION PROBLEM	DOSE TOO HIGH	DOSE TOO LOW	OTHER DOSE PROBLEM	TAKING TOO LITTLE	TAKING TOO MUCH	DIFFICULTY USING DOSAGE FORM	PATIENT USING OUT OF DATE MEDICATION	OTHER COMPLIANCE PROBLEM	CONDITION NOT ADEQUATELY TREATED	THERAPY REQUIRED	LABORATORY MONITORING	NON-LABORATORY MONITORING	OTHER MONITORING PROBLEM	PATIENT DRUG INFORMATION REQUEST	CONFUSION ABOUT THERAPY	DEMONSTRATION OF DEVICE	DISEASE MANAGEMENT OR ADVICE	OTHER EDUCATION OR INFORMATION PROBLEM	DIETARY PROBLEM	SMOKING PROBLEM	ALCOHOL PROBLEM	OTHER NON-CLINICAL PROBLEM	TOXICITY CAUSED BY DOSE	TOXICITY CAUSED BY DRUG INTERACTION	TOXICITY EVIDENT	OTHER TOXICITY/ADVERSE EFFECT PROBLEM	TOTAL
Antithrombotic agents	15	73			12	3		4		1	10	1			4	3	6	5			2					2		2	3	1	15	25	1	**188**
Drugs for peptic ulcer and gastro-oesophageal reflux disease (GORD)	6	7			34	5		24	2	2	3	2	4		3	16	2	38												1	4	24	2	**179**
Cholesterol and triglyceride reducers	4	37			4		1	9	7	3	6		2		4	26		22							1				2	2	3	28	1	**162**
Other analgesics and antipyretics		8				3		3	1	1	4	1	2		4	95	1	3											1	2	2	1		**132**
Oral blood glucose lowering drugs	2	4			6	17	1	10	1	3	9				2	19	4	24	1									2		4		14	1	**124**
Adrenergics, inhalants	7	2		2	5	1		4		1	21	2	21	1	2	26	1	4				5	6	1						1	5		**118**
Antiinflammatory and antirheumatic products, non-steroids	5	40			3	25		5	4		1				1	16		1				1			1						2	12	1	**118**
Beta blocking agents		13				9	4	2	1	1	4				6	22	3	6	3						1			1		2	8	24		**110**
Antidepressants	2	19			14	13		4	1	3	3				3	8	1					1								1	6	25		**104**
Ace inhibitors, plain		25			2	1		4	4		1				4	19	2	11								1					4	20		**98**
Opioids		9			1	5	2	2		1	2	2	3			51	3				1	1								2	1	12		**98**
High-ceiling diuretics	2	23			6	2		3	1		5					3	3	10												4	5	11		**78**
Angiotensin ii antagonists, plain		12			1	2		1	3		1				1	16		11	3						1					1	1	7		**61**
Antigout preparations	2	7			11	1		17			1	1				2		4														10		**56**
Cardiac glycosides	1	14						4	1	2	2					2		13		1										2	4	7		**53**
Vasodilators used in cardiac diseases	2	1			2		1	3		1	8		1	9	2	5	3					1			1		1			1	2	6		**50**
Selective calcium channel blockers with mainly vascular effects		2				3		1			3		1		1	15	1	1	1													20		**49**
Angiotensin ii antagonists, combinations	1	17			1	1	2	2								6	1	7												1	1	7		**47**
Other drugs for obstructive airway diseases, inhalants	7	2			1						7	1	8		2	5	1	1				1	1	1								9		**47**

	DRP type and subtype																																
	Drug selection							Over- and under-dose			Compliance and concordance					Untreated indications		Monitoring			Education					Non-clinical				Toxicity				
Drug group (ATC level III)	Duplication	Drug interaction	Wrong drug	Wrong dosage form	Unnecessary therapy/no apparent current indication	Contraindications apparent	Other drug selection problem	Dose too high	Dose too low	Other Dose Problem	Taking too little	Taking too much	Difficulty using dosage form	Patient using out of date medication	Other Compliance Problem	Condition not adequately treated	Therapy required	Laboratory Monitoring	Non-laboratory monitoring	Other Monitoring Problem	Patient drug information request	Confusion about therapy	Demonstration of device	Disease management or advice	Other Education or Information Problem	Dietary problem	Smoking problem	Alcohol problem	Other non-clinical problem	Toxicity caused by dose	Toxicity caused by drug interaction	Toxicity evident	Other Toxicity/Adverse Effect problem	Total
Drugs affecting bone structure and mineralization		2				4		2	1	1	4				4	15	4	2													6		**45**
Selective calcium channel blockers with direct cardiac effects		13		1	2	3		1	1		1		1		1	4	1										1			2	11		**43**
Calcium		12						2	2	5	1		2		3	6	2	3													1		**39**
Anxiolytics	2	1			1	13	1	4		1					2	4	1													1	7		**38**
Corticosteroids for systemic use, plain		6			1			2	1						1	2	8	3											3	1	10		**38**
Laxatives						6		3		1						12	2												4	2	5		**35**
Hypnotics and sedatives					1	16	1	3				1				3	2														6		**33**
Antipsychotics	1	1			2	6				3					2	2	2	5													6		**30**
Insulins and analogues		1			3			2	1	1	2				2	10	3																**25**
Antiepileptics		3			1	1				3						6	2	3		1										1	2		**23**
Vitamin a and d, incl. Combinations of the two	2	3			2			2	2			1			1	4	1	3													1		**22**
Low-ceiling diuretics, excl. Thiazides		5						3		1					2	4		1												1	4		**21**
Thyroid preparations	2	7					1			1		2			2		1	4											1				**21**
Cardiac stimulants excl. Cardiac glycosides	2	4			2			1			1		2	2	2			1												1	1		**19**
Potassium-sparing agents		5			2										1	1		4												3	3		**19**
Immunosuppressive agents		5				1		1	1							3		3													4		**18**
Potassium		4			2				1		2	1					1	6													1		**18**
Iron preparations		2			4				1		2					2		2				1						1	1				**16**
Antimetabolites		4				1		1	1							3		2													3		**15**
Antiadrenergic agents, peripherally acting					1	1				1					1	3		1	1										2	1	2		**14**
Antiarrhythmics, class i and iii		3											1			1	1	5													2		**13**
Other urologicals, incl. Antispasmodics		1				2				1		1				2					1										4		**12**

	DRP type and subtype																																
	Drug selection							Over- and under-dose			Compliance and concordance					Untreated indications		Monitoring			Education					Non-clinical				Toxicity				
Drug group (ATC level III)	Duplication	Drug interaction	Wrong drug	Wrong dosage form	Unnecessary therapy/no apparent current indication	Contraindications apparent	Other drug selection problem	Dose too high	Dose too low	Other Dose Problem	Taking too little	Taking too much	Difficulty using dosage form	Patient using out of date medication	Other Compliance Problem	Condition not adequately treated	Therapy required	Laboratory Monitoring	Non-Laboratory monitoring	Other Monitoring Problem	Patient drug information request	Confusion about therapy	Demonstration of device	Disease management or advice	Other Education or Information Problem	Dietary problem	Smoking problem	Alcohol problem	Other non-clinical problem	Toxicity caused by dose	Toxicity caused by drug interaction	Toxicity evident	Other Toxicity/Adverse Effect problem	Total
Ace inhibitors, combinations		7													1			1													2		**11**
Anti-dementia drugs		3				1										1									1					1	4		**11**
Antiglaucoma preparations and miotics1)	2	1			1	1					5					1																	**11**
Antimalarials		1				8																									2		**11**
Other mineral supplements		1			3	1			2	1						1		2															**11**
Antihistamines for systemic use		1			3	1	2									2															1		**10**
Bacterial vaccines																	9																**9**
Vitamin b12 and folic acid					2				2	1				1																	3		**9**
Corticosteroids, plain						1					3			1								1								1			**7**
Sulfonamides and trimethoprim		2	1			2												1													1		**7**
Antacids											1					2	1	1													1		**6**
Antiadrenergic agents, centrally acting					1						1					2		1													1		**6**
Estrogens					1			2							1	1														1			**6**
Dopaminergic agents		1									1				1			1													1		**5**
Other sex hormones and modulators of the genital system		1			1											1		2															**5**
Propulsives						1		1										1													2		**5**
Androgens		2																1													1		**4**
Decongestants and other nasal preparations for topical use											3																				1		**4**
Low-ceiling diuretics, thiazides	1	2																													1		**4**
Other antibacterials						3																									1		**4**
Antiinflammatory agents						2		1																									**3**
Antipropulsives													1			1														1			**3**

	DRP type and subtype																															
	Drug selection							Over- and under-dose			Compliance and concordance					Untreated indications		Monitoring			Education					Non-clinical				Toxicity				
Drug group (ATC level III)	Duplication	Drug interaction	Wrong drug	Wrong dosage form	Unnecessary therapy/no apparent current indication	Contraindications apparent	Other drug selection problem	Dose too high	Dose too low	Other Dose Problem	Taking too little	Taking too much	Difficulty using dosage form	Patient using out of date medication	Other Compliance Problem	Condition not adequately treated	Therapy required	Laboratory Monitoring	Non-Laboratory monitoring	Other Monitoring Problem	Patient drug information request	Confusion about therapy	Demonstration of device	Disease management or advice	Other Education or Information Problem	Dietary problem	Smoking problem	Alcohol problem	Other non-clinical problem	Toxicity caused by dose	Toxicity caused by drug interaction	Toxicity evident	Other Toxicity/Adverse Effect problem	Total
Arteriolar smooth muscle, agents acting on					1													2															**3**
Intestinal antiinflammatory agents																1						1										1	**3**
Multivitamins, combinations		1			1			1																									**3**
Other antianaemic preparations																1			1									1					**3**
Other ophthalmologicals							1							1		1																	**3**
Other systemic drugs for obstructive airway diseases					1						1							1															**3**
Anticholinergic agents					1																									1			**2**
Antipsoriatics for topical use																1		1															**2**
Ascorbic acid (vitamin c), incl. Combinations					2																												**2**
Beta-lactam antibacterials, penicillins					2																												**2**
Decongestants and antiallergics								1	1																								**2**
Muscle relaxants, centrally acting agents					1											1																	**2**
Tetracyclines					2																												**2**
Viral vaccines																	2																**2**
All other therapeutic products																	1																**1**
Antifungals for topical use											1																						**1**
Antiinfectives														1																			**1**
Antimycotics for systemic use		1																															**1**
Antiobesity preparations, excl. Diet products					1																												**1**
Antithyroid preparations																															1		**1**
Antivaricose therapy		1																															**1**
Antivertigo preparations	1																																**1**

Drug group (ATC level III)	DRP type and subtype																																		
	Drug selection							Over- and under-dose			Compliance and concordance					Untreated indications		Monitoring			Education					Non-clinical				Toxicity				
	Duplication	Drug interaction	Wrong drug	Wrong dosage form	Unnecessary therapy/no apparent current indication	Contraindications apparent	Other drug selection problem	Dose too high	Dose too low	Other Dose Problem	Taking too little	Taking too much	Difficulty using dosage form	Patient using out of date medication	Other Compliance Problem	Condition not adequately treated	Therapy required	Laboratory Monitoring	Non-Laboratory monitoring	Other Monitoring Problem	Patient drug information request	Confusion about therapy	Demonstration of device	Disease management or advice	Other Education or Information Problem	Dietary problem	Smoking problem	Alcohol problem	Other non-clinical problem	Toxicity caused by dose	Toxicity caused by drug interaction	Toxicity evident	Other Toxicity/Adverse Effect problem	Total
Belladonna and derivatives, plain																														1				1
Corticosteroids and antiinfectives in combination								1																										1
Diuretics and potassium-sparing agents in combination																														1				1
Drugs for functional bowel disorders																														1				1
Drugs used in addictive disorders																1																		1
Drugs used in benign prostatic hypertrophy																															1			1
Expectorants, excl. Combinations with cough suppressants					1																													1
Macrolides, lincosamides and streptogramins								1																										1
Other beta-lactam antibacterials									1																									1
Other plain vitamin preparations						1																												1
Progestogens					1																													1
Progestogens and oestrogens in combination						1																												1
Psychostimulants, agents used for adhd and nootropics																1																		1
Topical products for joint and muscular pain																1																		1
Total	**69**	**422**	**1**	**3**	**153**	**168**	**17**	**137**	**44**	**40**	**120**	**16**	**49**	**16**	**66**	**462**	**76**	**224**	**10**	**2**	**4**	**13**	**7**	**2**	**6**	**3**	**1**	**6**	**8**	**35**	**80**	**370**	**7**	**2637**

TABLE 152 - FREQUENCY OF RECOMMENDATIONS MADE TO RESOLVE DRPS ACCORDING TO CLASS OF DRUG INVOLVED IN DRP

	RECOMMENDATION TYPE																	
DRUG CLASS ASSOCIATED WITH DRP (ATC LEVEL III)	**LABORATORY MONITORING**	**NON-LABORATORY MONITORING**	**FOLLOW-UP BY PRESCRIBER**	**FOLLOW-UP BY ANOTHER**	**PATIENT/CARER EDUCATION**	**PRESCRIBER INFORMATION**	**COMPLIANCE ASSISTANCE**	**DOSE INCREASE**	**DOSE DECREASE**	**DRUG CEASE**	**DRUG START**	**FORMULATION CHANGE**	**DOSE SCHEDULE CHANGE**	**DRUG SWITCH**	**OTHER THERAPY CHANGE**	**NO RECOMMENDATION MADE**	**NO RECOMMENDATION NECESSARY**	**TOTAL**
Antithrombotic agents	37	23	10		12		5	5	7	62	17	5	2	25	1	1	13	**225**
Drugs for peptic ulcer and gastro-oesophageal reflux disease	61	3	7		4		2	13	44	34	12	3	5	21		1	5	**215**
Cholesterol and triglyceride reducers	59	6	7	1	6	1		18	13	19	22	3	6	16	1	2	8	**188**
Other analgesics and antipyretics	14		3		12		4	85	4	7	19	10	5	10			2	**175**
Antiinflammatory and antirheumatic products, non-steroids	17	3	2		6	1		22	10	27	21	3	2	35		1	7	**157**
Oral blood glucose lowering drugs	36	6	10		5	1	1	16	13	15	18	7	4	14			4	**150**
Opioids	4	4	4	1	6	1	2	44	8	10	22	3	7	25			2	**143**
Adrenergics, inhalants	6	1	10	1	21		14	5	8	16	19	12	5	14	1		6	**139**
Antidepressants	6	6	4	1	3	2	1	6	12	34	14	2	4	26		1	11	**133**
Beta blocking agents	13	12	5	1	9	1	3	10	11	10	10		9	22		1	16	**133**
Ace inhibitors, plain	31	4	3	2	6	1	1	14	5	17	10	2	2	19			6	**123**
High-ceiling diuretics	33	2	1	1	3			3	17	20	3		1	7			5	**96**
Angiotensin ii antagonists, plain	18	6			1	1	1	5	5	9	11		1	13			3	**74**
Antigout preparations	11	2	1	1	1		1		19	18	1	1		4	1		5	**66**
Selective calcium channel blockers with mainly vascular effects	3	5	1		3			9	5	5	12	1	3	16			3	**66**
Cardiac glycosides	37	2	1	1					5	3	1		3	3		2	2	**60**
Vasodilators used in cardiac diseases	2	1	10		9		1	2	4	4	4	1	4	6	2	1	4	**55**

Drug class associated with DRP (ATC level III)	Recommendation type																	
	Laboratory monitoring	Non-laboratory monitoring	Follow-up by prescriber	Follow-up by another	Patient/carer education	Prescriber information	Compliance assistance	Dose increase	Dose decrease	Drug cease	Drug start	Formulation change	Dose schedule change	Drug switch	Other therapy change	No recommendation made	No recommendation necessary	Total
Selective calcium channel blockers with direct cardiac effects	8	6	4	1	5	1	2	3	2	6	3	2		7			4	**54**
Angiotensin ii antagonists, combinations	18	4	1		3	1		1	2	2	3		1	10		1	6	**53**
Corticosteroids for systemic use, plain	11				1		1		3	13	15			7			2	**53**
Laxatives	1		2		3			13	5	9	12			8				**53**
Drugs affecting bone structure and mineralization	11	1	1	1	2		1	1		10	14	5	2	2			1	**52**
Other drugs for obstructive airway diseases, inhalants	1	2	1		12		3			7	8	3	1	7		1	6	**52**
Anxiolytics	3	2	1					3	11	7	3	1	1	13			3	**48**
Calcium	12	1			1			6	1	1	3	4	11	7			1	**48**
Hypnotics and sedatives	2	1	3	1	3			1	7	10	2		1	10		2	2	**45**
Antipsychotics	10	5	1	1			1	2	2	6	1	1	3	5		1	2	**41**
Antiepileptics	8		1			1		6		2	4		5	1			1	**29**
Low-ceiling diuretics, excl_ thiazides	6				1	1		1	4	5	2	3	2	3				**28**
Insulins and analogues	1			7	2			1		4	6		1	4			1	**27**
Vitamin a and d, incl_ combinations of the two	9	1						3	1	3	6	1		1				**25**
Potassium-sparing agents	11							1	5	4				3				**24**
Thyroid preparations	11		1		1		1		3	2		1	4					**24**
Cardiac stimulants excl_ cardiac glycosides	3	1	1		1				1	7		6					1	**21**
Immunosuppressive agents	6					1		1		4	5			3			1	**21**
Antiadrenergic agents, peripherally acting	2		1	1			1		5	1	3		1	4			1	**20**

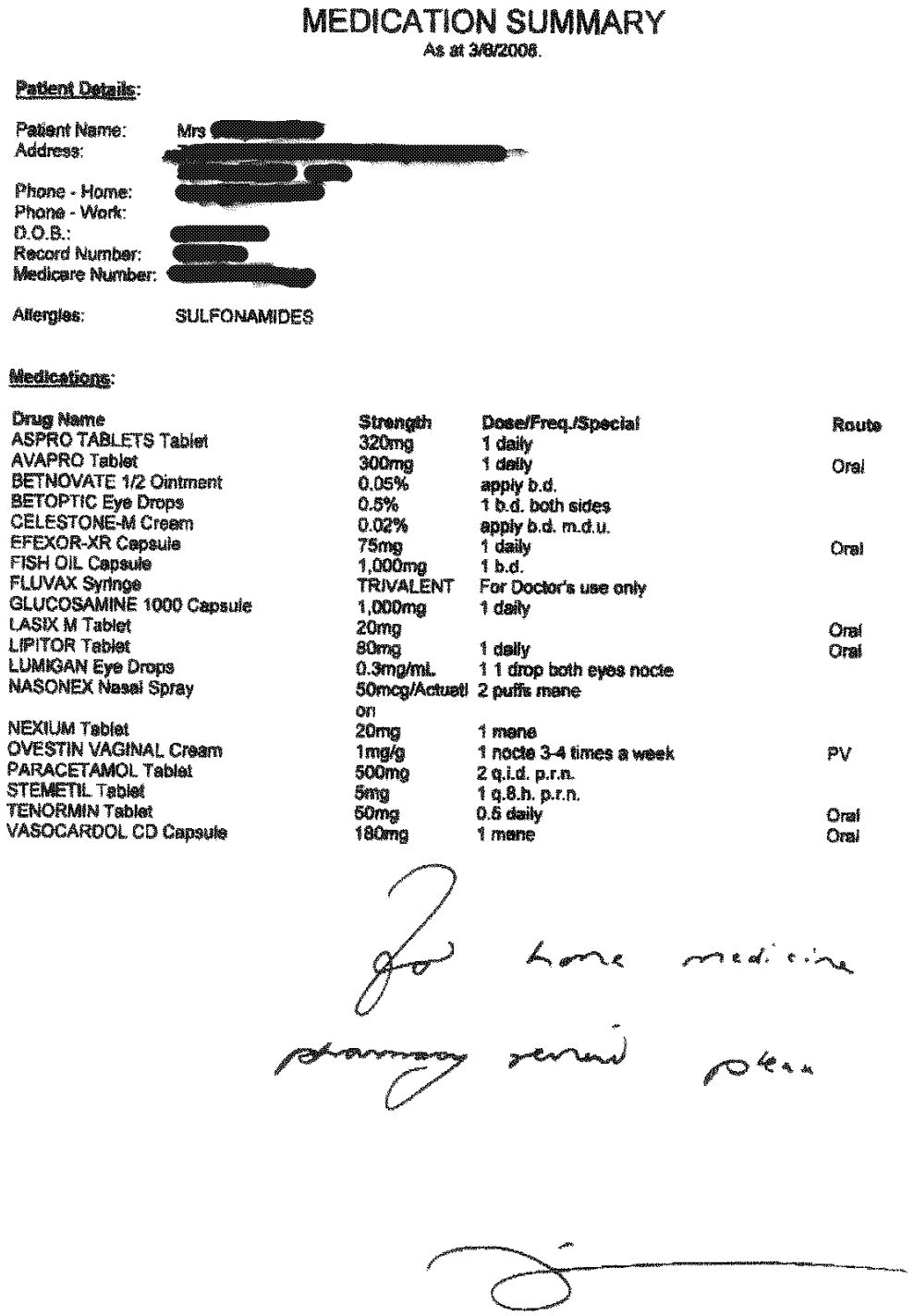
Drug class associated with DRP (ATC level III)	Recommendation type																	
	Laboratory monitoring	Non-laboratory monitoring	Follow-up by prescriber	Follow-up by another	Patient/carer education	Prescriber information	Compliance assistance	Dose increase	Dose decrease	Drug cease	Drug start	Formulation change	Dose schedule change	Drug switch	Other therapy change	No recommendation made	No recommendation necessary	Total
Potassium	12				1			2		3		1					1	**20**
Antimetabolites	4					1		1		4	5			3				**18**
Iron preparations	5		2						1	3	2	1	2					**16**
Ace inhibitors, combinations	4	1			1		1	1	1	1				3			2	**15**
Other urologicals, incl_ antispasmodics					3				3	5	1		1	1			1	**15**
Other mineral supplements	5	1		2				4		2								**14**
Antiarrhythmics, class i and iii	7	1						1			2	1				1		**13**
Antimalarials	3		1						1	4				3			1	**13**
Anti-dementia drugs	1	3			1			1	2	1	1		1				1	**12**
Antiglaucoma preparations and miotics1)		1		3	3		1			3								**11**
Antihistamines for systemic use		1			1				3	2	1			2				**10**
Bacterial vaccines			1					1			7							**9**
Sulfonamides and trimethoprim	4		1			1				1				2				**9**
Vitamin b12 and folic acid	2		2					2	1	2								**9**
Antiadrenergic agents, centrally acting	1				1			1			2			1			2	**8**
Corticosteroids, plain			3		3			1									1	**8**
Estrogens			1		1				2	3							1	**8**
Propulsives	1								1	2				3			1	**8**
Antacids	1		1		1			1						2		1		**7**

Drug class associated with DRP (ATC level III)	Recommendation type																		
	Laboratory monitoring	Non-laboratory monitoring	Follow-up by prescriber	Follow-up by another	Patient/carer education	Prescriber information	Compliance assistance	Dose increase	Dose decrease	Drug cease	Drug start	Formulation change	Dose schedule change	Drug switch	Other therapy change	No recommendation made	No recommendation necessary	Total
Decongestants and other nasal preparations for topical use							1	1						4				**6**
Dopaminergic agents	1							1				1	1	1			1	**6**
Other antibacterials								1	1					4				**6**
Low-ceiling diuretics, thiazides	1			1						3								**5**
Other sex hormones and modulators of the genital system	3										1			1				**5**
Androgens	3																1	**4**
Antiinflammatory agents		1												3				**4**
Antipropulsives					1			1	1					1				**4**
Intestinal antiinflammatory agents			2							1				1				**4**
Muscle relaxants, centrally acting agents								2		1		1						**4**
Other systemic drugs for obstructive airway diseases	1				1					2								**4**
Anticholinergic agents					1					1				1				**3**
Arteriolar smooth muscle, agents acting on	2									1								**3**
Multivitamins, combinations					1				1	1								**3**
Other antianaemic preparations		1	1								1							**3**
Other ophthalmologicals							1				1			1				**3**
Psychostimulants, agents used for adhd and nootropics								1	1				1					**3**
Antipsoriatics for topical use	1										1							**2**
Ascorbic acid										2								**2**

Drug class associated with DRP (ATC level III)	Recommendation type																		
	Laboratory monitoring	Non-laboratory monitoring	Follow-up by prescriber	Follow-up by another	Patient/carer education	Prescriber information	Compliance assistance	Dose increase	Dose decrease	Drug cease	Drug start	Formulation change	Dose schedule change	Drug switch	Other therapy change	No recommendation made	No recommendation necessary	Total
Belladonna and derivatives, plain											1			1				**2**
Beta-lactam antibacterials, penicillins										2								**2**
Decongestants and antiallergics								1						1				**2**
Drugs for functional bowel disorders											1			1				**2**
Progestogens and oestrogens in combination	1													1				**2**
Tetracyclines										2								**2**
Viral vaccines											2							**2**
All other therapeutic products											1							**1**
Antifungals for topical use					1													**1**
Antiinfectives					1													**1**
Antimycotics for systemic use	1																	**1**
Antiobesity preparations, excl_ diet products										1								**1**
Antithyroid preparations																	1	**1**
Antivaricose therapy		1																**1**
Antivertigo preparations			1															**1**
Corticosteroids and antiinfectives in combination										1								**1**
Diuretics and potassium-sparing agents in combination														1				**1**
Drugs used in addictive disorders								1										**1**
Drugs used in benign prostatic hypertrophy										1								**1**

Drug class associated with DRP (ATC level III)	Recommendation type																	
	Laboratory monitoring	Non-laboratory monitoring	Follow-up by prescriber	Follow-up by another	Patient/carer education	Prescriber information	Compliance assistance	Dose increase	Dose decrease	Drug cease	Drug start	Formulation change	Dose schedule change	Drug switch	Other therapy change	No recommendation made	No recommendation necessary	Total
Expectorants, excl_ combinations with cough suppressants														1				1
Macrolides, lincosamides and streptogramins									1									1
Other beta-lactam antibacterials								1										1
Other plain vitamin preparations										1								1
Progestogens										1								1
Topical products for joint and muscular pain								1										1
Total	**586**	**121**	**113**	**28**	**164**	**16**	**50**	**327**	**262**	**470**	**336**	**85**	**102**	**414**	**6**	**17**	**148**	**3245**

Appendix XX - Examples of referrals according to definitions used for stratification



MEDICATION SUMMARY
As at 3/8/2006.

Patient Details:

Patient Name: Mrs [redacted]
Address: [redacted]
Phone - Home: [redacted]
Phone - Work:
D.O.B.: [redacted]
Record Number: [redacted]
Medicare Number: [redacted]

Allergies: SULFONAMIDES

Medications:

Drug Name	Strength	Dose/Freq./Special	Route
ASPRO TABLETS Tablet	320mg	1 daily	
AVAPRO Tablet	300mg	1 daily	Oral
BETNOVATE 1/2 Ointment	0.05%	apply b.d.	
BETOPTIC Eye Drops	0.5%	1 b.d. both sides	
CELESTONE-M Cream	0.02%	apply b.d. m.d.u.	
EFEXOR-XR Capsule	75mg	1 daily	Oral
FISH OIL Capsule	1,000mg	1 b.d.	
FLUVAX Syringe	TRIVALENT	For Doctor's use only	
GLUCOSAMINE 1000 Capsule	1,000mg	1 daily	
LASIX M Tablet	20mg		Oral
LIPITOR Tablet	80mg	1 daily	Oral
LUMIGAN Eye Drops	0.3mg/mL	1 1 drop both eyes nocte	
NASONEX Nasal Spray	50mcg/Actuati on	2 puffs mane	
NEXIUM Tablet	20mg	1 mane	
OVESTIN VAGINAL Cream	1mg/g	1 nocte 3-4 times a week	PV
PARACETAMOL Tablet	500mg	2 q.i.d. p.r.n.	
STEMETIL Tablet	5mg	1 q.8.h. p.r.n.	
TENORMIN Tablet	50mg	0.5 daily	Oral
VASOCARDOL CD Capsule	180mg	1 mane	Oral

FIGURE 65 - HMR REFERRAL WITH "MINIMAL" MEDICAL HISTORY AND "IRRELEVANT, LIMITED OR ABSENT" PATHOLOGY/ LABORATORY RESULTS

Referral for Domiciliary Medication Management - Home Medicines Review

Medical Benefits Schedule Item 900. Also known as DMMR or HMR

Thursday, 24 July 2008

Patient	Community Pharmacy	General Practitioner
M[redacted] [redacted] [redacted] Phone: [redacted] DoB: [redacted] Medicare no: DVA no: [redacted]	[redacted] [redacted] [redacted] Phone: [redacted] Fax: [redacted] E-mail:	Dr [redacted] [redacted] [redacted] [redacted] Phone: [redacted] Fax. [redacted] E-mail: Provider no: [redacted] Prescriber no: [redacted]

Medical History

Active:

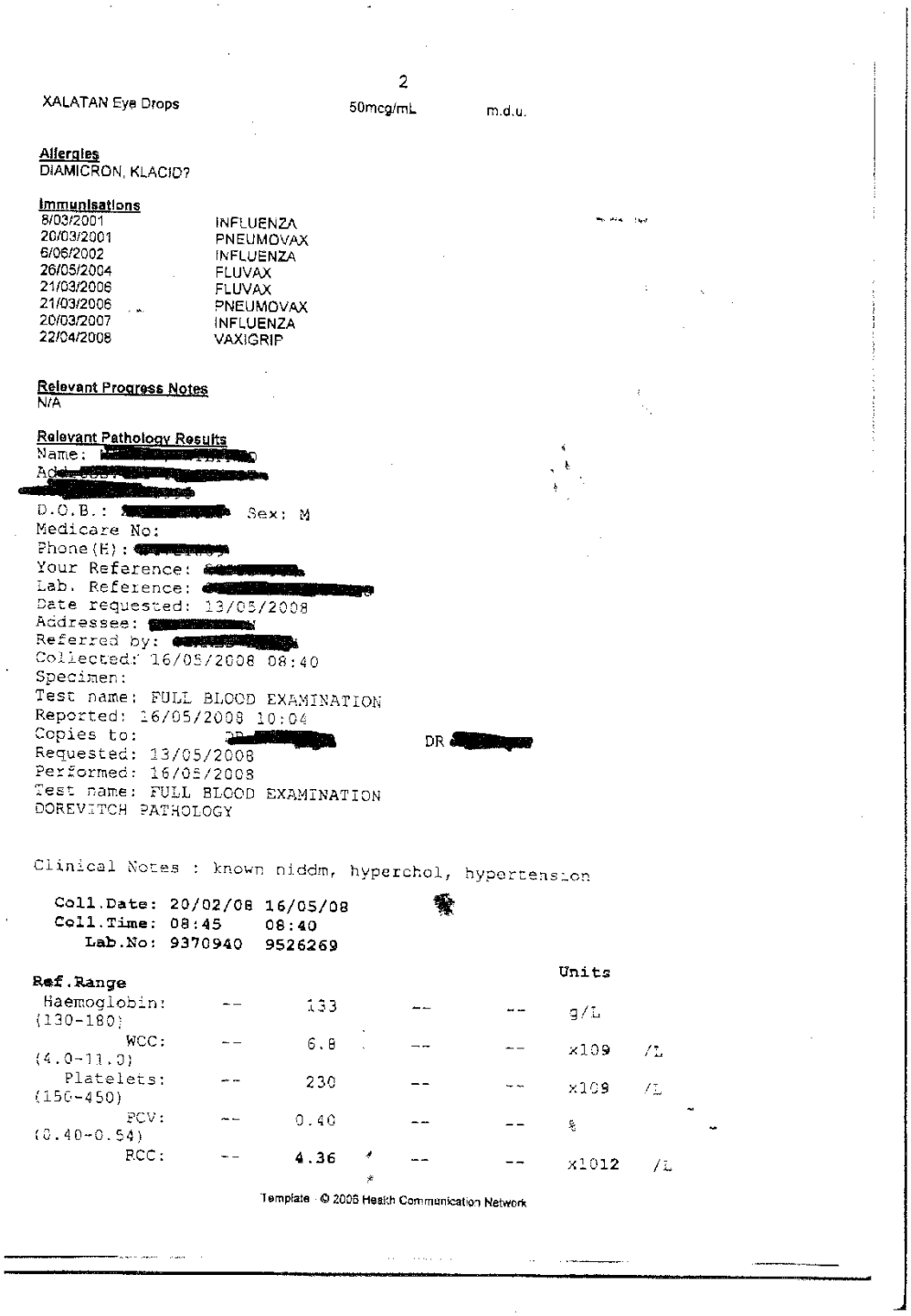
Date	Condition -- Comment
	IHD (ISCHAEMIC HEART DISEASE)
1998	CABG (CORONARY ARTERY BYPASS GRAFT) first bypass at the [redacted] 30 years ago. Last one at [redacted] 4 years ago
2001	DIABETES MELLITUS - NIDDM
2001	HYPERTENSION
2001	OSTEOARTHRITIS
2003	CAROTID ARTERY OCCLUSION(Right)
2003	DEPRESSION
2003	SENSORINEURAL DEAFNESS(Bilateral)
2004	AAA REPAIR
2004	CELLULITIS - LEG(Right)
2004	PACEMAKER-DUAL CHAMBER
2005	DIABETES MELLITUS - NIDDM
2005	RENAL STONE

Inactive:

Date	Condition -- Comment
	TURP Had twice 1993 and 15 years ago with worse symptoms
2001	ASTHMA
2001	BLEPHAROPLASTY UPR EYELIDS(Bilateral)
2002	1 ST DEGREE HEART BLOCK
2002	POSTERIOR RHINITIS
2002	TRIFASCICULAR BLOCK
2003	BELLS PALSY(Right)
2004	BRADYARRHYTHMIA
2008	CYST - KIDNEY needs FU USS May 2008
2008	IMPINGEMENT SYNDROME (OF [redacted]OULDER)(Left)
2008	L 3RD NERVE PALSY, ACUTE seen by Dr [redacted], possible due to old R ICA occlusion

Current Medications

Drug Name	Strength	Dose/Freq./Special
ATACAND Tablet	16mg	1 nocte
CRESTOR Tablet	5mg	1 daily
DIABEX XR Sr Tablet	500mg	1 b.d.
FELODUR ER Tablet	10mg	1 tab daily
GLUCOSAMINE HYDROCHLORIDE Tablet	750mg	1 b.d.
LASIX Tablet	40mg	1 mane and at midday
MONODUR Tablet	60mg	1/2 b.d.
NITROLINGUAL PUMPSPRAY Spray	400mcg/dose	1 p.r.n.
PANADOL OSTEO Tablet	665mg	2 b.d.
SOLPRIN Disp'tablet	300mg	1/2 mane c.c.



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XALATAN Eye Drops 50mcg/mL m.d.u.

Allergies
DIAMICRON, KLACID?

Immunisations

8/03/2001	INFLUENZA
20/03/2001	PNEUMOVAX
6/06/2002	INFLUENZA
26/05/2004	FLUVAX
21/03/2006	FLUVAX
21/03/2006	PNEUMOVAX
20/03/2007	INFLUENZA
22/04/2008	VAXIGRIP

Relevant Progress Notes
N/A

Relevant Pathology Results
Name: [redacted]
Ad[redacted]
[redacted]
D.O.B.: [redacted] Sex: M
Medicare No:
Phone(H): [redacted]
Your Reference: [redacted]
Lab. Reference: [redacted]
Date requested: 13/05/2008
Addressee: [redacted]
Referred by: [redacted]
Collected: 16/05/2008 08:40
Specimen:
Test name: FULL BLOOD EXAMINATION
Reported: 16/05/2008 10:04
Copies to: [redacted] DR [redacted]
Requested: 13/05/2008
Performed: 16/05/2008
Test name: FULL BLOOD EXAMINATION
DOREVITCH PATHOLOGY

Clinical Notes : known niddm, hyperchol, hypertension

Coll.Date:	**20/02/08**	**16/05/08**				
Coll.Time:	**08:45**	**08:40**				
Lab.No:	**9370940**	**9526269**				
Ref.Range					**Units**	
Haemoglobin: (130-180)	--	133	--	--	g/L	
WCC: (4.0-11.0)	--	6.8	--	--	x109	/L
Platelets: (150-450)	--	230	--	--	x109	/L
PCV: (0.40-0.54)	--	0.40	--	--	%	
RCC:	--	4.36	--	--	x1012	/L

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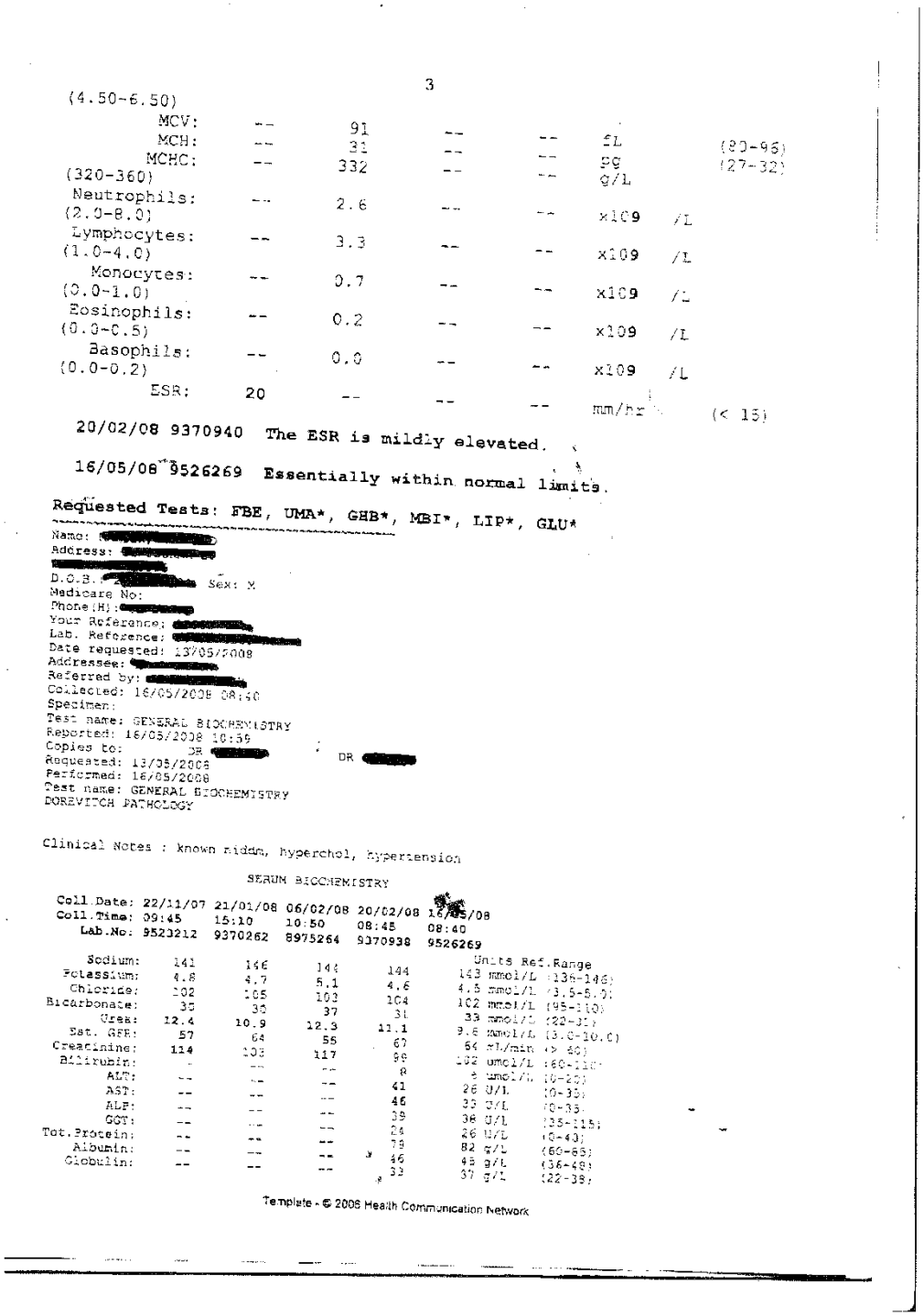

3

(4.50-6.50)						
MCV:	--	91	--	--	fL	(80-96)
MCH:	--	31	--	--	pg	(27-32)
MCHC: (320-360)	--	332	--	--	g/L	
Neutrophils: (2.0-8.0)	--	2.6	--	--	x109 /L	
Lymphocytes: (1.0-4.0)	--	3.3	--	--	x109 /L	
Monocytes: (0.0-1.0)	--	0.7	--	--	x109 /L	
Eosinophils: (0.0-0.5)	--	0.2	--	--	x109 /L	
Basophils: (0.0-0.2)	--	0.0	--	--	x109 /L	
ESR:	20	--	--	--	mm/hr	(< 15)

20/02/08 9370940 The ESR is mildly elevated.

16/05/08 9526269 Essentially within normal limits.

Requested Tests: FBE, UMA*, GHB*, MBI*, LIP*, GLU*

Name: [redacted]
Address: [redacted]
D.O.B. [redacted] Sex: M
Medicare No:
Phone(H): [redacted]
Your Reference: [redacted]
Lab. Reference: [redacted]
Date requested: 13/05/2008
Addressee: [redacted]
Referred by: [redacted]
Collected: 16/05/2008 08:40
Specimen:
Test Name: GENERAL BIOCHEMISTRY
Reported: 16/05/2008 10:59
Copies to: DR [redacted] DR [redacted]
Requested: 13/05/2008
Performed: 16/05/2008
Test name: GENERAL BIOCHEMISTRY
DOREVITCH PATHOLOGY

Clinical Notes : known riddm, hyperchol, hypertension

SERUM BIOCHEMISTRY

	Coll.Date:	22/11/07	21/01/08	06/02/08	20/02/08	16/05/08	Units	Ref.Range
	Coll.Time:	09:45	15:10	10:50	08:45	08:40		
	Lab.No:	9523212	9370262	8975264	9370938	9526269		
Sodium:		141	146	143	144	143	mmol/L	(136-146)
Potassium:		4.8	4.7	5.1	4.6	4.5	mmol/L	(3.5-5.0)
Chloride:		102	105	103	104	102	mmol/L	(95-110)
Bicarbonate:		30	30	37	31	33	mmol/L	(22-31)
Urea:		12.4	10.9	12.3	11.1	9.6	mmol/L	(3.0-10.0)
Est. GFR:		57	64	56	67	64	mL/min	(> 60)
Creatinine:		114	103	117	99	102	umol/L	(60-110)
Bilirubin:		-	--	--	8	6	umol/L	(0-20)
ALT:		--	--	--	41	26	U/L	(0-35)
AST:		--	--	--	46	33	U/L	(0-35)
ALP:		--	--	--	99	98	U/L	(35-115)
GGT:		--	--	--	24	26	U/L	(0-40)
Tot.Protein:		--	--	--	79	82	g/L	(60-85)
Albumin:		--	--	--	46	45	g/L	(36-48)
Globulin:		--	--	--	33	37	g/L	(22-38)

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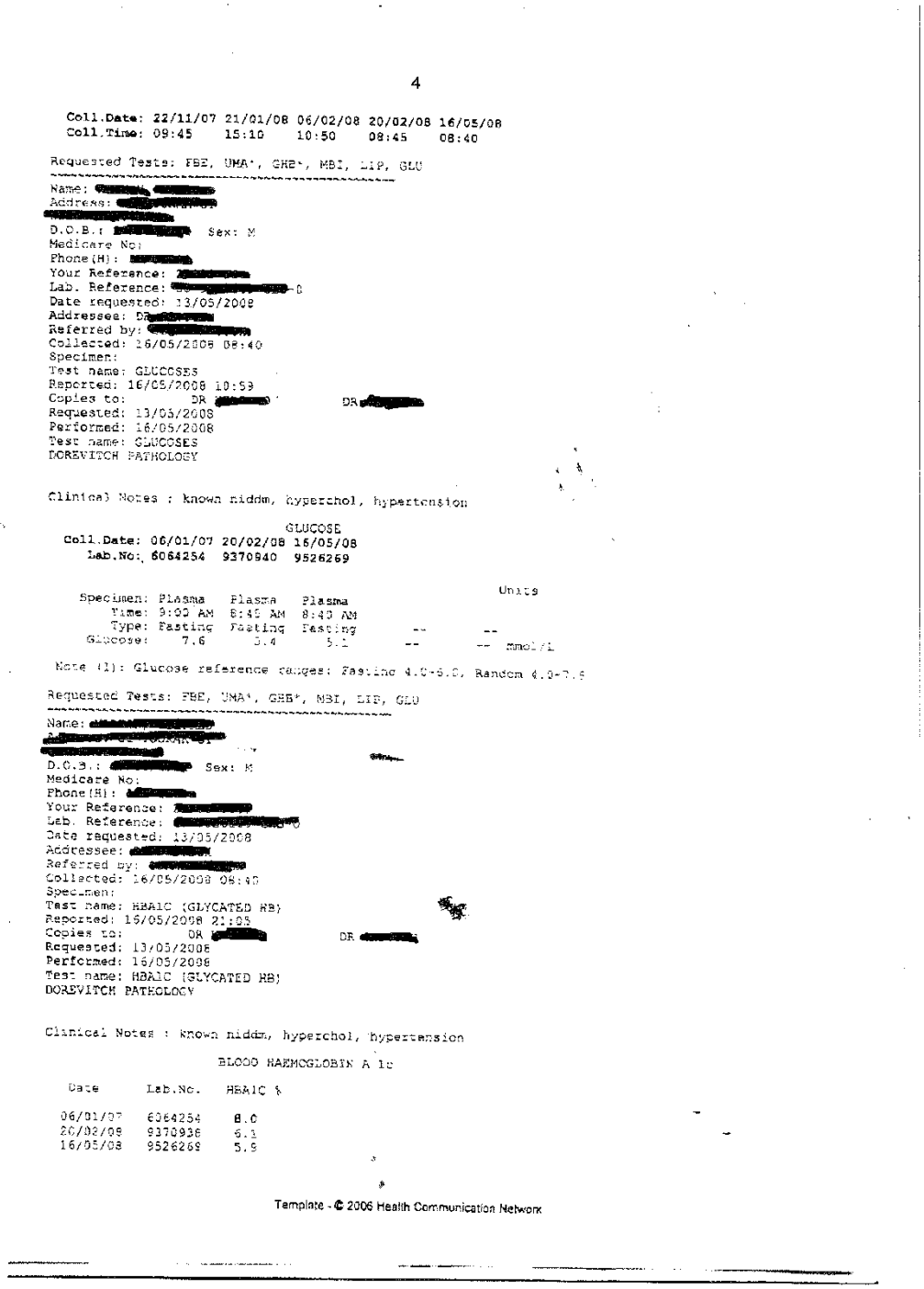

4

Coll.Date: 22/11/07 21/01/08 06/02/08 20/02/08 16/05/08
Coll.Time: 09:45 15:10 10:50 08:45 08:40

Requested Tests: FBE, UMA*, GHB*, MBI, LIP, GLU

Name: [redacted]
Address: [redacted]

D.O.B.: [redacted] Sex: M
Medicare No:
Phone(H): [redacted]
Your Reference: [redacted]
Lab. Reference: [redacted]
Date requested: 13/05/2008
Addressee: DR [redacted]
Referred by: [redacted]
Collected: 16/05/2008 08:40
Specimen:
Test name: GLUCOSES
Reported: 16/05/2008 10:59
Copies to: DR [redacted] DR [redacted]
Requested: 13/05/2008
Performed: 16/05/2008
Test name: GLUCOSES
DOREVITCH PATHOLOGY

Clinical Notes : known niddm, hyperchol, hypertension

GLUCOSE

Coll.Date: 06/01/07 20/02/08 16/05/08
Lab.No: 6064254 9370940 9526269

Specimen:	Plasma	Plasma	Plasma			Units
Time:	9:00 AM	8:45 AM	8:40 AM			
Type:	Fasting	Fasting	Fasting	--	--	
Glucose:	7.6	5.4	5.1	--	--	mmol/L

Note (1): Glucose reference ranges: Fasting 4.0-6.0, Random 4.0-7.8

Requested Tests: FBE, UMA*, GHB*, MBI, LIP, GLU

Name: [redacted]
[redacted]
D.O.B.: [redacted] Sex: M
Medicare No:
Phone(H): [redacted]
Your Reference: [redacted]
Lab. Reference: [redacted]
Date requested: 13/05/2008
Addressee: [redacted]
Referred by: [redacted]
Collected: 16/05/2008 08:40
Specimen:
Test name: HBA1C (GLYCATED HB)
Reported: 16/05/2008 21:05
Copies to: DR [redacted] DR [redacted]
Requested: 13/05/2008
Performed: 16/05/2008
Test name: HBA1C (GLYCATED HB)
DOREVITCH PATHOLOGY

Clinical Notes : known niddm, hyperchol, hypertension

BLOOD HAEMOGLOBIN A 1c

Date	Lab.No.	HBA1C %
06/01/07	6064254	8.0
20/02/08	9370938	6.1
16/05/08	9526269	5.9

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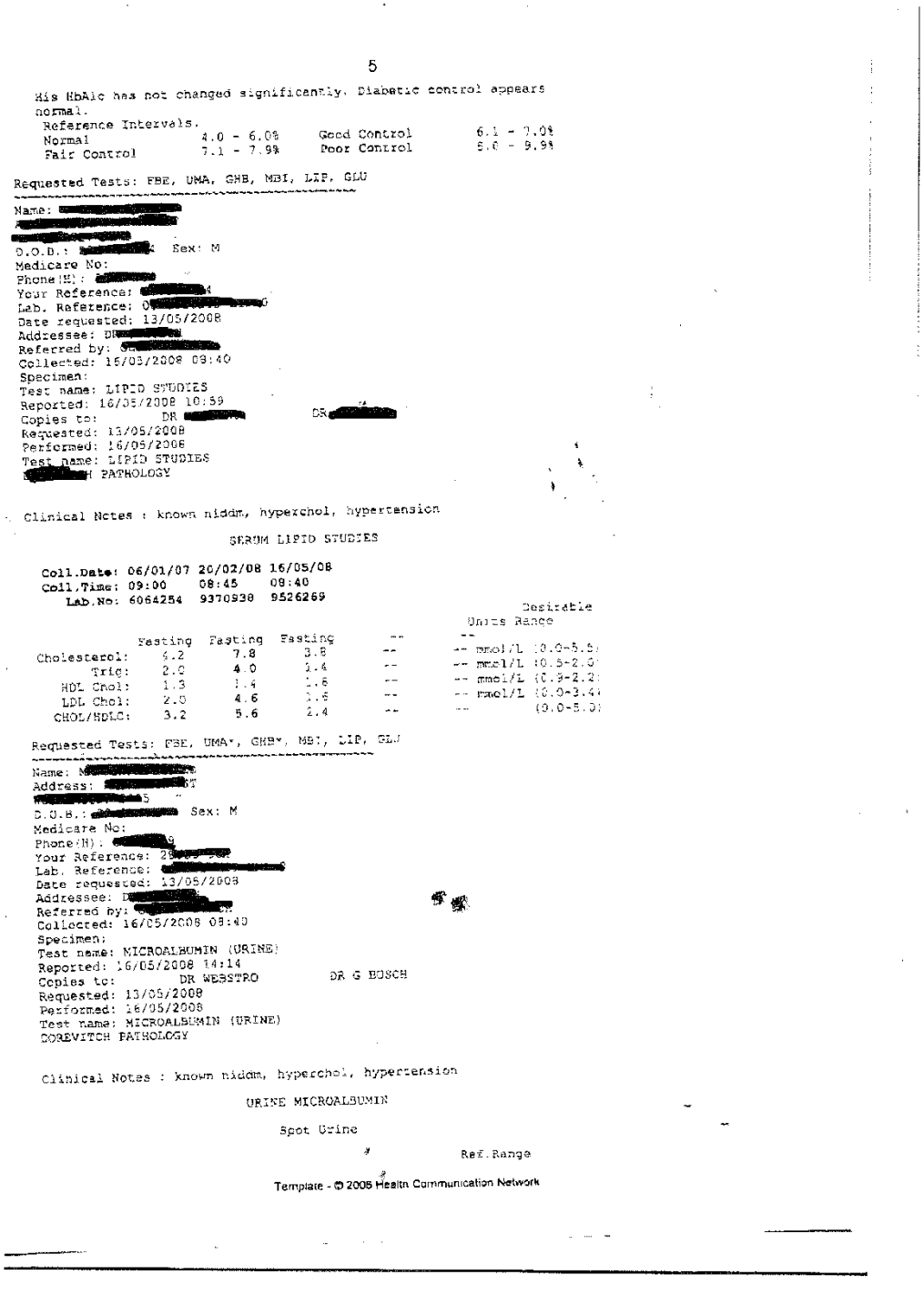

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His HbAlc has not changed significantly. Diabetic control appears normal.

Reference Intervals.

Normal	4.0 - 6.0%	Good Control	6.1 - 7.0%
Fair Control	7.1 - 7.9%	Poor Control	8.0 - 9.9%

Requested Tests: FBE, UMA, GHB, MBI, LIP, GLU

Name: [redacted]
D.O.B.: [redacted] Sex: M
Medicare No:
Phone(H): [redacted]
Your Reference: [redacted]
Lab. Reference: [redacted]
Date requested: 13/05/2008
Addressee: DR [redacted]
Referred by: [redacted]
Collected: 16/05/2008 08:40
Specimen:
Test name: LIPID STUDIES
Reported: 16/05/2008 10:59
Copies to: DR [redacted] DR [redacted]
Requested: 13/05/2008
Performed: 16/05/2008
Test name: LIPID STUDIES
[redacted] PATHOLOGY

Clinical Notes : known niddm, hyperchol, hypertension

SERUM LIPID STUDIES

	Coll.Date:	06/01/07	20/02/08	16/05/08		Desirable Units Range
	Coll.Time:	09:00	08:45	09:40		
	Lab.No:	6064254	9370938	9526269		
		Fasting	Fasting	Fasting	--	--
Cholesterol:		6.2	7.8	3.8	--	-- mmol/L (3.0-5.5)
Trig:		2.0	4.0	1.4	--	-- mmol/L (0.5-2.0)
HDL Chol:		1.3	1.4	1.6	--	-- mmol/L (0.9-2.2)
LDL Chol:		2.0	4.6	1.6	--	-- mmol/L (0.0-3.4)
CHOL/HDLC:		3.2	5.6	2.4	--	-- (0.0-5.0)

Requested Tests: FBE, UMA*, GHB*, MBI, LIP, GLU

Name: [redacted]
Address: [redacted]
D.O.B.: [redacted] Sex: M
Medicare No:
Phone(H): [redacted]
Your Reference: [redacted]
Lab. Reference: [redacted]
Date requested: 13/05/2008
Addressee: [redacted]
Referred by: [redacted]
Collected: 16/05/2008 08:40
Specimen:
Test name: MICROALBUMIN (URINE)
Reported: 16/05/2008 14:14
Copies to: DR WEBSTRO DR G BOSCH
Requested: 13/05/2008
Performed: 16/05/2008
Test name: MICROALBUMIN (URINE)
COREVITCH PATHOLOGY

Clinical Notes : known niddm, hyperchol, hypertension

URINE MICROALBUMIN

Spot Urine

Ref.Range

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Albumin Concentration:	22	mg/L	(0-25)
Creatinine Concentration:	6.8	mmol/L	
Alb/Creat Ratio (ACR):	3.2	mg/mmol creat	(< 2.5)

Requested Tests: FBE, UMA, GHB*, MBI, LFP, GLU

Measurements

Date	BP (Sitting)	BP (Standing)	Height	Pulse (Sitting)	Weight

16/02/2007	150/80	
20/02/2007	150/80	
1/03/2007	120/80	
20/03/2007	120/80	
27/04/2007	130/70	
3/05/2007	120/80	
18/05/2007	140/80	
24/09/2007	120/80	
24/10/2007	120/80	
6/12/2007	120/70	
14/01/2008	130/80	
6/02/2008	116/70	68
6/02/2008	116/70	72
22/04/2008	140/80	
13/05/2008	118/70	
24/07/2008	140/65	60

Social History	**Occupation**
lives with wife, has 8 children	retired

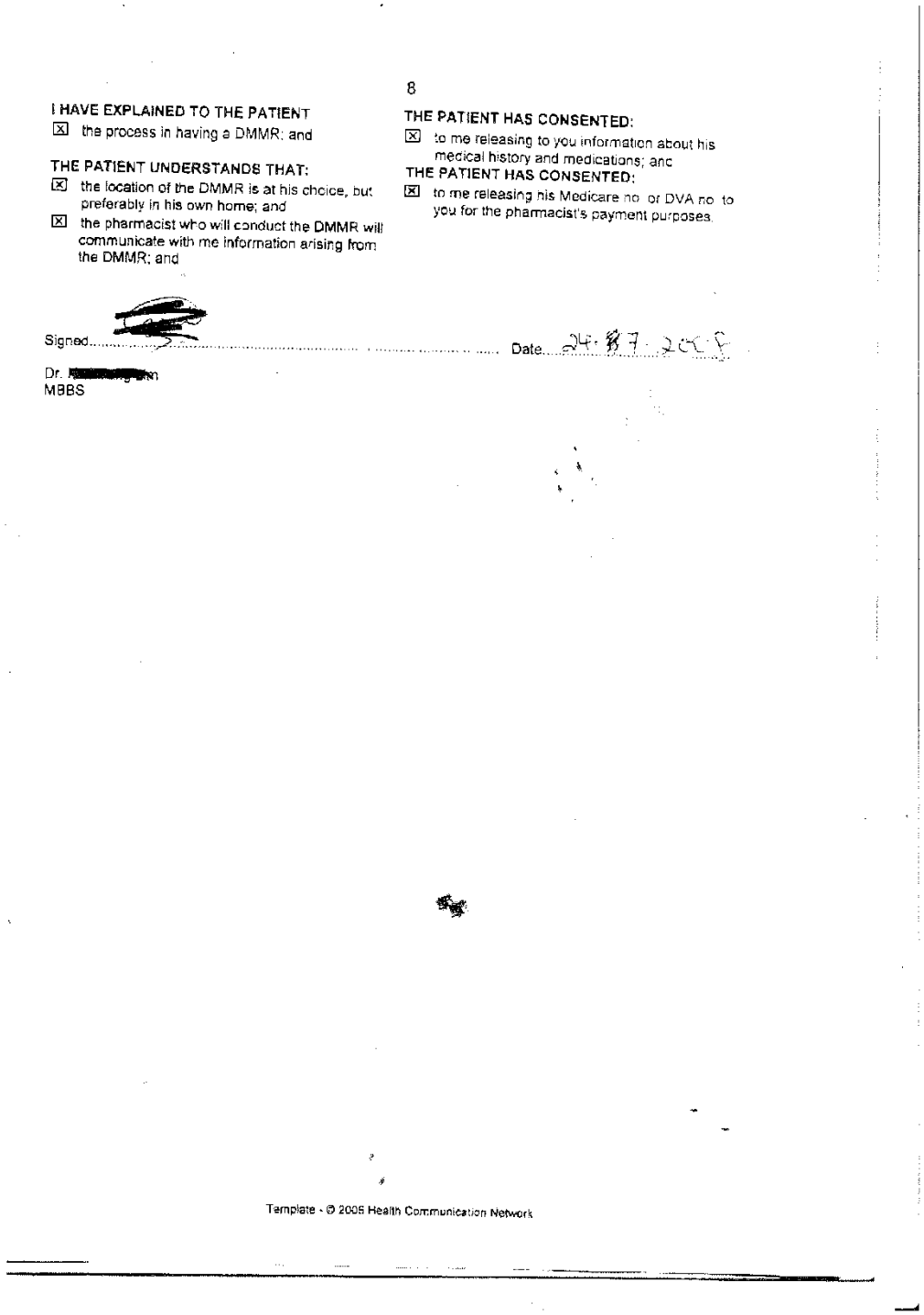
Smoking status	**Alcohol consumption**
Ex-smoker Quitting stage:	Unknown

Reason for referral for DMMR	**Issues that may influence medication use**
Currently taking 5 or more regular medications Taking more than 12 doses of medication per day	*To select any item - highlight its checkbox and type x* ☐ poor vision ☐ hearing problems ☐ swallowing difficulties ☐ dexterity ☐ language and/or literacy problems ☐ cognition ☐ other: *please specify...*

Medication Administration	**Dosing Aids**
Medication usually administered by him/her self	☐ dosing aid device e.g. Dosett, Webster. *Specify brand or type...* ☐ other: *please specify...* If a dosing aid is used, it is filled by
Disease Monitoring Devices	**Medication Administration Devices**
☐ peak flow meter ☐ BP monitor ☐ blood glucose meter ☐ INR monitor ☐ other: *please specify...*	☐ spacer device for respiratory inhalers ☐ nebuliser pump for respiratory solutions ☐ other: *please specify...*

The patient speaks enough English to do the interview.

An interpreter is not required. The patient's preferred language is English.



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I HAVE EXPLAINED TO THE PATIENT
☒ the process in having a DMMR; and

THE PATIENT UNDERSTANDS THAT:
☒ the location of the DMMR is at his choice, but preferably in his own home; and
☒ the pharmacist who will conduct the DMMR will communicate with me information arising from the DMMR; and

THE PATIENT HAS CONSENTED:
☒ to me releasing to you information about his medical history and medications; and

THE PATIENT HAS CONSENTED:
☒ to me releasing his Medicare no or DVA no to you for the pharmacist's payment purposes.

Signed..... Date.. 24.07.2009

Dr. [redacted]
MBBS

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FIGURE 66 - HMR REFERRAL WITH "DETAILED" MEDICAL HISTORY AND "RECENT AND POTENTIALLY RELEVANT" PATHOLOGY/ LABORATORY DATA

Appendix XXI - Example calculation of potential economic value

Introduction

The following worked example illustrates how the estimates of QOL and health resource utilisation with and without each HMR were calculated. The patient reviewed (HMR 11) was an 87 year old male whose medical history included glaucoma, gout, high cholesterol, hypertension, osteoarthritis, renal impairment and type II diabetes. The patient was referred for a HMR as part of the DVA dosage administration program, and a HMR was performed on 24 May 2008. His medications at the time of the HMR and their estimated costs are shown in Table 153.

TABLE 153 - MEDICATION PROFILE AND ESTIMATED MONTHLY DRUG COSTS

BRAND	GENERIC INGREDIENT/S	DOSE	ESTIMATED MONTHLY COST TO PBS ($)
Allosig 100mg Tab	Allopurinol	100mg in the morning	0.86
Avapro 300mg Tab	Irbesartan	300mg in the morning	24.81
Codalgin Forte Tab	Paracetamol and codeine	One tablet when required	-PRN, not costed-
Coloxyl with Senna Tab	Docusate and senna	One tablet when required	-PRN, not costed-
Coversyl 5mg Tab	Perindopril	5mg at night	13.64
Diamicron 80mg Tab	Gliclazide	80mg in the morning	2.70
Hydraderm Cream	Urea	Applied when required	-PRN, not costed-
Lipidil 145mg Tab	Fenofibrate	145mg at night	36.32
MagMin 500mg Tab	Magnesium aspartate	500mg at night	-not PBS listed-
Minax 50mg Tab	Metoprolol	50mg in the morning	1.62
Panamax 500mg Tab	Paracetamol	0.5-1.0mg every four hours when required	-PRN, not costed-
Plavix 75mg Tab	Clopidogrel	75mg in the morning	77.79
Polaramine 2mg Tab	Dexchlorphenirimine	2mg when required	-PRN, not costed-
Simvar 40mg Tab	Simvastatin	40mg at night	39.02
Xalatan Eye Drops 0.005%	Latanoprost	One drop into the right eye at night	33.62
TOTAL			**230.38**

The laboratory and pathology data provided with the HMR referral are shown in Table 154.

TABLE 154 - LABORATORY AND PATHOLOGY DATA PROVIDED WITH HMR REFERRAL

DATE	PARAMETER	VALUE	REFERENCE RANGE
	Diabetes		
09-May-08	Glycosylated Hb (HbA1c)	5.9	< 7.0%
	Haematology		
09-May-08	Ferritin	500	25-300 mcg/L
09-May-08	Haemoglobin	147	130-170 g/L
09-May-08	Iron	21.4	11-24 micromol/L
09-May-08	Mean cellular volume (MCV)	94	82-98 fL
09-May-08	Packed cell volume (PCV, HCT)	0.45	0.4-0.52
09-May-08	Platelet count	255	150-400 x 10^9/L
09-May-08	Red cell count - Male	4.79	4.4-5.9 x 10^{12}/L
09-May-08	Transferrin	2.78	20-45 micromol/L
09-May-08	Transferrin saturation	31	15-55%
09-May-08	White cell differential count	6.4	4-11 x 10^9/L
	Lipid studies		
09-May-08	Total cholesterol (fasting)	4.9	< 4.0 mmol/L
09-May-08	Triglycerides	2.1	< 2.0 mmol/L
	Liver function tests		
09-May-08	Alanine aminotransferase (ALT)	20	< 36 U/L
09-May-08	Albumin (serum)	41	35-50 g/L
09-May-08	Alkaline phosphatase (total)	66	35-135 U/L
09-May-08	Aspartate Aminotransferase (AST)	23	< 40 U/L
09-May-08	Bilirubin (total)	8	< 20micromol/L
09-May-08	Gamma glutamyl transpeptidase (γGT)	24	< 60 U/L
09-May-08	Protein (Total, serum)	71	60-80 g/L
	Observations		
01-Apr-08	Blood pressure	140/70	mmHg
13-May-08	Blood pressure	144/72	mmHg
13-Feb-08	Blood pressure	140/80	mmHg
14-Jan-08	Albumin:creatinine ratio	45.3	0.1-2.3 mg/mmol
	Urea and electrolytes		
09-May-08	Bicarbonate (serum)	24	22-32 mmol/L
09-May-08	Calcium (corrected)	2.36	2.10-2.55 mmol/L
09-May-08	Chloride	112	95-110mmol/L
09-May-08	Creatinine	222	50-120 micromol/L
09-May-08	Phosphate (inorganic)	1.05	0.7-1.7 mmol/L
09-May-08	Potassium (serum)	4.8	3.5-5.0 mmol/L
09-May-08	Sodium (serum)	146	138-145 mmol/L
09-May-08	Urea	13.1	2.2-7.7 mmol/L

DRPs assessed

The pharmacist documented the following DRPs and recommendations in the HMR report. A summary of the outcomes data provided for each DRPs is also presented.

1. DRP 53 - subtype: *Dose too high*

The pharmacist reported that the patient had renal impairment and was taking a dose of fenofibrate above that recommended for his level of renal impairment. A dose reduction to 96mg daily was recommended, which was implemented by the GP.

2. DRP 54 - subtype: *Laboratory monitoring*

The pharmacist noted that the patient was taking a magnesium supplement which may accumulate due to his renal impairment. Monitoring of magnesium levels was recommended, which was performed by the GP.

3. DRP 55 - subtype: *Drug interaction*

It was reported that the combination of fenofibrate and simvastatin is associated with a high risk of myopathy and rhabdomyolysis, particularly in elderly patients with renal impairment. The pharmacist recommended monitoring for muscle pain, tenderness and weakness, and to check creatine kinase levels if these symptoms occur. The GP ordered a creatine kinase level to be performed.

Calculation of potential economic value

The potential costs and QOL effects of the HMRs were calculated in a series of steps that integrated the results of the expert assessment of the interventions made by the pharmacist in the HMR, with the estimated changes in drug costs resulting from these interventions. Essentially, the methodology used the changes in drug costs and the experts' estimates of consequences and their before- and after-intervention probabilities to calculate initial values for the outcomes of each HMR. The outcomes data (whether or not the pharmacists' recommendations were implemented) and attribution estimates were then used to assign appropriate portions of the difference

between the before- and after-intervention costs and QOL effects to create final estimates of these parameters with- and without- the HMR.

Step 1 - Calculation of drug cost changes

The changes in drug costs were estimated by calculating the total cost of each drug that would have been commenced or ceased as a result of each of the pharmacist's recommendations. In this example, the pharmacist's recommendations to resolve DRP 53 resulted in the cessation of the 145mg strength of fenofibrate, with commencement of the 96mg strength. No other drug cost changes occurred as a result of this HMR. The costs associated with these changes are shown in Table 155.

TABLE 155 - CALCULATION OF CHANGE IN MONTHLY DRUG COSTS

DRP	DRUG/S	PBS CODE	STARTED OR CEASED	CHANGE IN MONTHLY COST TO PBS ($)
114	Fenofibrate 145mg tablets	9247Q	Cease	-36.32
	Fenofibrate 48mg tablets	9246P	Start	24.62
Total				**-11.70**

Hence, this HMR resulted in a total decrease in monthly drug costs of $11.70, equating to $140.40 annually. This value was incorporated into the calculation after Step 2, in which the healthcare resource utilisation costs and QOL effects of the interventions were calculated.

Step 2 - Calculation of health resource utilisation and QOL effects in the absence of any intervention

The results of the expert assessment of the recommendations made to resolve the DRPs were used in the following steps. The consequences the experts selected and their before- and after- probabilities are shown in Table 156. All 15 experts assessed this HMR, and none indicated that there was insufficient information to predict the likely outcomes resulting from it.

TABLE 156 - AVERAGED EXPERT ESTIMATES OF ATTRIBUTION AND CONSEQUENCES SELECTED FOR HMR 11

DRP	PARAMETER	AVERAGE ESTIMATED PROBABILITY (% LIKELIHOOD)					
		MILD		MODERATE		SEVERE	
		BEFORE	AFTER	BEFORE	AFTER	BEFORE	AFTER
53	Liver Disease	0.1	0	0.1	0	0	0
	Myopathy	7.5	3.7	4	2.2	1.1	0.6
	Renal Dysfunction	10.7	7.5	9.3	6.4	4	1.7
	Attribution			60.7			
54	Confusion	0.7	0.3	0.3	0.1	0.3	0.1
	Diarrhoea	1.3	1	0.7	0.5	0.1	0.1
	Myopathy	0.3	0.3	0.1	0.1	0	0
	Renal Dysfunction	2.3	0.7	0.7	0.1	0.1	0
	Attribution			64.1			
55	Liver Disease	3.3	2.1	3	0.7	3.3	0.8
	Myopathy	10.1	4.8	5.2	2.5	3.4	0.8
	Rash	0.3	0	0.2	0	0.1	0
	Attribution			50.8			

To generate the estimate of the health resource utilisation and QOL effects that would have occurred in the absence of any intervention, the experts' before-intervention probability estimates were used. Each parameter in the consequences table that described the health states that had been selected (for example, GP visits, hospitalisation costs *et cetera*), was multiplied by the experts' before-intervention probability estimates. The result of this multiplication was the health resource utilisation and QOL effects that would have occurred in the absence of any intervention.

The consequence table parameter values are shown for the consequences selected by the experts for HMR 11 in Table 157. The results of multiplying the experts' before-intervention probability estimates by the values in Table 157 are shown in Table 158 (the before-intervention scenario).

TABLE 157 - CONSEQUENCE TABLE VALUES FOR THE CONSEQUENCES SELECTED BY EXPERTS FOR DRPS ADDRESSED IN HMR 11

CONSEQUENCE	DAYS OF ILL HEALTH			NUMBER (COST, $) OF PHYSICIAN VISITS						COST OF LABORATORY/ PATHOLOGY TESTS ($)			DURATION (COST, $) OF HOSPITALISATION			QOL (QALY)		
				GP			SPECIALIST											
	MILD	MODERATE	SEVERE	MILD	MODERATE	SEVERE	MILD	MODERATE	SEVERE	MILD	MODERATE	SEVERE	MILD	MODERATE	SEVERE	MILD	MODERATE	SEVERE
Confusion	0.0	17.3	60.0	2.0 (67.10)	4.0 (134.20)	5.0 (167.75)	0.0 (0.00)	1.0 (79.05)	0.0 (3.08)	138.15	226.80	329.19	0.0 (0.00)	0.0 (0.00)	7.6 (5662.98)	1.000	0.978	0.845
Diarrhoea	0.0	7.9	14.3	1.0 (33.55)	2.0 (67.10)	4.0 (134.20)	0.0 (0.00)	0.0 (0.00)	0.0 (1.72)	71.61	102.75	121.98	0.0 (0.00)	0.0 (0.00)	2.1 (4220.00)	1.000	0.998	0.975
Liver disease	0.0	0.1	50.1	1.0 (33.55)	4.0 (134.20)	6.0 (201.30)	0.0 (0.00)	1.0 (79.05)	5.0 (237.85)	30.45	101.36	121.10	0.0 (0.00)	0.0 (0.00)	4.1 (4058.04)	1.000	1.000	0.866
Myopathy	0.1	13.1	31.9	1.0 (33.55)	3.0 (100.65)	5.0 (167.75)	0.0 (0.00)	0.0 (0.00)	2.0 (118.75)	17.40	51.91	110.36	0.0 (0.00)	0.0 (0.00)	0.0 (0.00)	1.000	0.986	0.901
Rash	0.0	12.1	48.2	1.0 (33.55)	3.0 (100.65)	4.0 (134.20)	0.0 (0.00)	1.0 (79.05)	4.0 (198.15)	0.00	25.60	47.15	0.0 (0.00)	0.0 (0.00)	2.5 (2220.69)	1.000	0.990	0.873
Renal dysfunction	0.0	0.1	53.2	2.0 (67.10)	4.0 (134.20)	6.0 (201.30)	0.0 (0.00)	1.0 (79.05)	4.0 (198.15)	42.99	126.55	176.23	0.0 (0.00)	0.0 (0.00)	6.5 (6395.05)	1.000	1.000	0.924

TABLE 158 - EXPERTS' ESTIMATES OF OUTCOMES OF CONSEQUENCES WITHOUT ANY INTERVENTION FOR HMR 11

DRP	CONSEQUENCE	DAYS OF ILL HEALTH			NUMBER (COST, $) OF PHYSICIAN VISITS						COST OF LABORATORY/ PATHOLOGY TESTS ($)			DURATION (COST, $) OF HOSPITALISATION			QOL (QALY)		
					GP			SPECIALIST											
		MILD	MODERATE	SEVERE	MILD	MODERATE	SEVERE	MILD	MODERATE	SEVERE	MILD	MODERATE	SEVERE	MILD	MODERATE	SEVERE	MILD	MODERATE	SEVERE
53	Liver Disease	0.0	0.0	0.0	0.0 (0.03)	0.0 (0.13)	0.0 (0.00)	0.0 (0.00)	0.0 (0.08)	0.0 (0.00)	0.0	0.1	0.0	0.0 (0.00)	0.0 (0.00)	0.0 (0.00)	1.000	1.000	1.000
	Myopathy	0.0	0.5	0.4	0.1 (2.52)	0.1 (4.03)	0.1 (1.85)	0.0 (0.00)	0.0 (0.00)	0.0 (1.31)	1.3	2.1	1.2	0.0 (0.00)	0.0 (0.00)	0.0 (0.00)	1.000	0.999	0.999
	Renal Dysfunction	0.0	0.0	2.1	0.2 (7.18)	0.4 (12.48)	0.2 (8.05)	0.0 (0.00)	0.1 (7.35)	0.2 (7.93)	4.6	11.8	7.0	0.0 (0.00)	0.0 (0.00)	0.3 (255.80)	1.000	1.000	0.997
	Total	0.0	0.5	2.5	0.3 (9.73)	0.5 (16.64)	0.3 (9.90)	0.0 (0.00)	0.1 (7.43)	0.2 (9.23)	5.9	13.9	8.3	0.0 (0.00)	0.0 (0.00)	0.3 (255.80)	1.000	0.999	0.996
54	Confusion	0.0	0.1	0.2	0.0 (0.47)	0.0 (0.40)	0.0 (0.50)	0.0 (0.00)	0.0 (0.24)	0.0 (0.01)	1.0	0.7	1.0	0.0 (0.00)	0.0 (0.00)	0.0 (16.99)	1.000	1.000	1.000
	Diarrhoea	0.0	0.1	0.0	0.0 (0.44)	0.0 (0.47)	0.0 (0.13)	0.0 (0.00)	0.0 (0.00)	0.0 (0.00)	0.9	0.7	0.1	0.0 (0.00)	0.0 (0.00)	0.0 (4.22)	1.000	1.000	1.000
	Myopathy	0.0	0.0	0.0	0.0 (0.10)	0.0 (0.10)	0.0 (0.00)	0.0 (0.00)	0.0 (0.00)	0.0 (0.00)	0.1	0.1	0.0	0.0 (0.00)	0.0 (0.00)	0.0 (0.00)	1.000	1.000	1.000
	Renal Dysfunction	0.0	0.0	0.1	0.0 (1.54)	0.0 (0.94)	0.0 (0.20)	0.0 (0.00)	0.0 (0.55)	0.0 (0.20)	1.0	0.9	0.2	0.0 (0.00)	0.0 (0.00)	0.0 (6.40)	1.000	1.000	1.000
	Total	0.0	0.1	0.2	0.1 (2.55)	0.1 (1.91)	0.0 (0.84)	0.0 (0.00)	0.0 (0.79)	0.0 (0.21)	2.9	2.3	1.3	0.0 (0.00)	0.0 (0.00)	0.0 (27.60)	1.000	1.000	0.999
55	Liver Disease	0.0	0.0	1.7	0.0 (1.11)	0.1 (4.03)	0.2 (6.64)	0.0 (0.00)	0.0 (2.37)	0.2 (7.85)	1.0	3.0	4.0	0.0 (0.00)	0.0 (0.00)	0.1 (133.92)	1.000	1.000	0.996
	Myopathy	0.0	0.7	1.1	0.1 (3.39)	0.2 (5.23)	0.2 (5.70)	0.0 (0.00)	0.0 (0.00)	0.1 (4.04)	1.8	2.7	3.8	0.0 (0.00)	0.0 (0.00)	0.0 (0.00)	1.000	0.999	0.997
	Rash	0.0	0.0	0.0	0.0 (0.10)	0.0 (0.20)	0.0 (0.13)	0.0 (0.00)	0.0 (0.16)	0.0 (0.20)	0.0	0.1	0.0	0.0 (0.00)	0.0 (0.00)	0.0 (2.22)	1.000	1.000	1.000
	Total	0.0	0.7	2.8	0.1 (4.60)	0.3 (9.46)	0.4 (12.48)	0.0 (0.00)	0.0 (2.53)	0.2 (12.08)	2.8	5.8	7.8	0.0 (0.00)	0.0 (0.00)	0.1 (136.14)	1.000	0.999	0.992
Total		**0.0**	**1.4**	**5.5**	**0.5 (16.88)**	**0.8 (28.01)**	**0.7 (23.22)**	**0.0 (0.00)**	**0.1 (10.75)**	**0.4 (21.53)**	**11.6**	**22.1**	**17.3**	**0.0 (0.00)**	**0.0 (0.00)**	**0.4 (419.54)**	**1.000**	**0.999**	**0.987**

Step 3 - Calculation of health resource utilisation and QOL effects after the interventions

The next step involved generation of the estimated health resource utilisation and QOL effects that would have occurred after the interventions that were valued in the model (that is, the HMR and the other healthcare providers). This step used the experts' after-intervention probability estimates. As with the previous step, each parameter in the consequences table that described the health states that had been selected was multiplied by the experts' after-intervention probability estimates. The result of this multiplication was the health resource utilisation and QOL effects that were estimated to have occurred due to every intervention made in the 12 months following the HMR (shown in Table 159).

Table 160 shows the difference between the before- and after-intervention estimates, which are termed *total value* of the outcomes considered (for example, GP visits, hospitalisation costs, QOL *et cetera*) for HMR 11.

It should be noted that for simplicity, the values shown in these calculations are averages of the parameters in the consequences table and not distributions as used in the economic analysis calculations. Consequently, the values shown differ slightly to those in Table 163 and Table 164 as these were calculated using the distributions in the consequences table.

TABLE 159 - EXPERTS' ESTIMATES OF OUTCOMES OF CONSEQUENCES WITHOUT ANY INTERVENTION FOR HMR 11

DRP	CONSEQUENCE	DAYS OF ILL HEALTH			NUMBER (COST, $) OF PHYSICIAN VISITS						COST OF LABORATORY/ PATHOLOGY TESTS ($)			DURATION (COST, $) OF HOSPITALISATION			QOL (QALY)		
					GP			SPECIALIST											
		MILD	MODERATE	SEVERE	MILD	MODERATE	SEVERE	MILD	MODERATE	SEVERE	MILD	MODERATE	SEVERE	MILD	MODERATE	SEVERE	MILD	MODERATE	SEVERE
53	Liver Disease	0.0	0.0	0.0	0.0 (0.00)	0.0 (0.00)	0.0 (0.00)	0.0 (0.00)	0.0 (0.00)	0.0 (0.00)	0.0	0.0	0.0	0.0 (0.00)	0.0 (0.00)	0.0 (0.00)	1.000	1.000	1.000
	Myopathy	0.0	0.3	0.2	0.0 (1.24)	0.1 (2.21)	0.0 (1.01)	0.0 (0.00)	0.0 (0.00)	0.0 (0.71)	0.6	1.1	0.7	0.0 (0.00)	0.0 (0.00)	0.0 (0.00)	1.000	1.000	0.999
	Renal Dysfunction	0.0	0.0	0.9	0.2 (5.03)	0.3 (8.59)	0.1 (3.42)	0.0 (0.00)	0.1 (5.06)	0.1 (3.37)	3.2	8.1	3.0	0.0 (0.00)	0.0 (0.00)	0.1 (108.72)	1.000	1.000	0.999
	Total	0.0	0.3	1.1	0.2 (6.27)	0.3 (10.80)	0.1 (4.43)	0.0 (0.00)	0.1 (5.06)	0.1 (4.08)	3.9	9.2	3.7	0.0 (0.00)	0.0 (0.00)	0.1 (108.72)	1.000	1.000	0.998
54	Confusion	0.0	0.0	0.1	0.0 (0.20)	0.0 (0.13)	0.0 (0.17)	0.0 (0.00)	0.0 (0.08)	0.0 (0.00)	0.4	0.2	0.3	0.0 (0.00)	0.0 (0.00)	0.0 (5.66)	1.000	1.000	1.000
	Diarrhoea	0.0	0.0	0.0	0.0 (0.34)	0.0 (0.34)	0.0 (0.13)	0.0 (0.00)	0.0 (0.00)	0.0 (0.00)	0.7	0.5	0.1	0.0 (0.00)	0.0 (0.00)	0.0 (4.22)	1.000	1.000	1.000
	Myopathy	0.0	0.0	0.0	0.0 (0.10)	0.0 (0.10)	0.0 (0.00)	0.0 (0.00)	0.0 (0.00)	0.0 (0.00)	0.1	0.1	0.0	0.0 (0.00)	0.0 (0.00)	0.0 (0.00)	1.000	1.000	1.000
	Renal Dysfunction	0.0	0.0	0.0	0.0 (0.47)	0.0 (0.13)	0.0 (0.00)	0.0 (0.00)	0.0 (0.08)	0.0 (0.00)	0.3	0.1	0.0	0.0 (0.00)	0.0 (0.00)	0.0 (0.00)	1.000	1.000	1.000
	Total	0.0	0.1	0.1	0.0 (1.11)	0.0 (0.70)	0.0 (0.30)	0.0 (0.00)	0.0 (0.16)	0.0 (0.00)	1.5	0.9	0.5	0.0 (0.00)	0.0 (0.00)	0.0 (9.88)	1.000	1.000	1.000
55	Liver Disease	0.0	0.0	0.4	0.0 (0.70)	0.0 (0.94)	0.0 (1.61)	0.0 (0.00)	0.0 (0.55)	0.0 (1.90)	0.6	0.7	1.0	0.0 (0.00)	0.0 (0.00)	0.0 (32.46)	1.000	1.000	0.999
	Myopathy	0.0	0.3	0.3	0.0 (1.61)	0.1 (2.52)	0.0 (1.34)	0.0 (0.00)	0.0 (0.00)	0.0 (0.95)	0.8	1.3	0.9	0.0 (0.00)	0.0 (0.00)	0.0 (0.00)	1.000	1.000	0.999
	Rash	0.0	0.0	0.0	0.0 (0.00)	0.0 (0.00)	0.0 (0.00)	0.0 (0.00)	0.0 (0.00)	0.0 (0.00)	0.0	0.0	0.0	0.0 (0.00)	0.0 (0.00)	0.0 (0.00)	1.000	1.000	1.000
	Total	0.0	0.3	0.7	0.1 (2.31)	0.1 (3.46)	0.1 (2.95)	0.0 (0.00)	0.0 (0.55)	0.1 (2.85)	1.5	2.0	1.9	0.0 (0.00)	0.0 (0.00)	0.0 (32.46)	1.000	1.000	0.998
Total		0.0	0.7	1.8	0.3 (9.70)	0.4 (14.96)	0.2 (7.68)	0.0 (0.00)	0.1 (5.77)	0.1 (6.94)	6.8	12.2	6.0	0.0 (0.00)	0.0 (0.00)	0.2 (151.06)	1.000	0.999	0.996

TABLE 160 - DIFFERENCE BETWEEN THE TOTAL QOL AND HEALTH RESOURCE UTILISATION ESTIMATES BEFORE- AND AFTER-INTERVENTION FOR HMR 11

DRP	CONSEQUENCE	DAYS OF ILL HEALTH			NUMBER (COST, $) OF PHYSICIAN VISITS						COST OF LABORATORY/ PATHOLOGY TESTS ($)			DURATION (COST, $) OF HOSPITALISATION			QOL LOST (QALY)		
					GP			SPECIALIST											
		MILD	MODERATE	SEVERE	MILD	MODERATE	SEVERE	MILD	MODERATE	SEVERE	MILD	MODERATE	SEVERE	MILD	MODERATE	SEVERE	MILD	MODERATE	SEVERE
53	Liver Disease	0.0	0.0	0.0	0.0 (0.03)	0.0 (0.13)	0.0 (0.00)	0.0 (0.00)	0.0 (0.08)	0.0 (0.00)	0.0	0.1	0.0	0.0 (0.00)	0.0 (0.00)	0.0 (0.00)	0.000	0.000	0.000
	Myopathy	0.0	0.2	0.2	0.0 (1.27)	0.1 (1.81)	0.0 (0.84)	0.0 (0.00)	0.0 (0.00)	0.0 (0.59)	0.7	0.9	0.6	0.0 (0.00)	0.0 (0.00)	0.0 (0.00)	0.000	0.000	0.000
	Renal Dysfunction	0.0	0.0	1.2	0.1 (2.15)	0.1 (3.89)	0.1 (4.63)	0.0 (0.00)	0.0 (2.29)	0.1 (4.56)	1.4	3.7	4.1	0.0 (0.00)	0.0 (0.00)	0.2 (147.09)	0.000	0.000	-0.002
	Total	0.0	0.2	1.4	0.1 (3.46)	0.2 (5.84)	0.2 (5.47)	0.0 (0.00)	0.0 (2.37)	0.1 (5.15)	2.1	4.7	4.6	0.0 (0.00)	0.0 (0.00)	0.2 (147.09)	0.000	0.000	-0.002
54	Confusion	0.0	0.0	0.1	0.0 (0.27)	0.0 (0.27)	0.0 (0.34)	0.0 (0.00)	0.0 (0.16)	0.0 (0.01)	0.6	0.5	0.7	0.0 (0.00)	0.0 (0.00)	0.0 (11.33)	0.000	0.000	0.000
	Diarrhoea	0.0	0.0	0.0	0.0 (0.10)	0.0 (0.13)	0.0 (0.00)	0.0 (0.00)	0.0 (0.00)	0.0 (0.00)	0.2	0.2	0.0	0.0 (0.00)	0.0 (0.00)	0.0 (0.00)	0.000	0.000	0.000
	Myopathy	0.0	0.0	0.0	0.0 (0.00)	0.0 (0.00)	0.0 (0.00)	0.0 (0.00)	0.0 (0.00)	0.0 (0.00)	0.0	0.0	0.0	0.0 (0.00)	0.0 (0.00)	0.0 (0.00)	0.000	0.000	0.000
	Renal Dysfunction	0.0	0.0	0.1	0.0 (1.07)	0.0 (0.81)	0.0 (0.20)	0.0 (0.00)	0.0 (0.47)	0.0 (0.20)	0.7	0.8	0.2	0.0 (0.00)	0.0 (0.00)	0.0 (6.40)	0.000	0.000	0.000
	Total	0.0	0.1	0.2	0.0 (1.44)	0.0 (1.21)	0.0 (0.54)	0.0 (0.00)	0.0 (0.63)	0.0 (0.20)	1.5	1.4	0.8	0.0 (0.00)	0.0 (0.00)	0.0 (17.72)	0.000	0.000	0.000
55	Liver Disease	0.0	0.0	1.3	0.0 (0.40)	0.1 (3.09)	0.2 (5.03)	0.0 (0.00)	0.0 (1.82)	0.1 (5.95)	0.4	2.3	3.0	0.0 (0.00)	0.0 (0.00)	0.1 (101.45)	0.000	0.000	-0.003
	Myopathy	0.0	0.4	0.8	0.1 (1.78)	0.1 (2.72)	0.1 (4.36)	0.0 (0.00)	0.0 (0.00)	0.1 (3.09)	0.9	1.4	2.9	0.0 (0.00)	0.0 (0.00)	0.0 (0.00)	0.000	0.000	-0.003
	Rash	0.0	0.0	0.0	0.0 (0.10)	0.0 (0.20)	0.0 (0.13)	0.0 (0.00)	0.0 (0.16)	0.0 (0.20)	0.0	0.1	0.0	0.0 (0.00)	0.0 (0.00)	0.0 (2.22)	0.000	0.000	0.000
	Total	0.0	0.4	2.1	0.1 (2.28)	0.2 (6.01)	0.3 (9.53)	0.0 (0.00)	0.0 (1.98)	0.2 (9.23)	1.3	3.8	5.9	0.0 (0.00)	0.0 (0.00)	0.1 (103.67)	0.000	0.000	-0.006
Total		0.0	0.7	3.7	0.2 (7.18)	0.4 (13.05)	0.5 (15.53)	0.0 (0.00)	0.1 (4.98)	0.3 (14.59)	4.8	9.9	11.4	0.0 (0.00)	0.0 (0.00)	0.3 (268.48)	0	0	-0.008

Step 4 - Incorporation of outcomes data into the model

The next step incorporated the outcomes data into the calculation. All of the *total outcomes* calculated in the previous step were multiplied by a factor (termed *u*) based on whether or not the recommendation/s made for each DRP were implemented. The multiplication factors essentially discounted the *total outcomes* for every intervention, as follows:

- for recommendations that were implemented, the *u* value was 1.0 (that is, there was no discount that needed to be applied since it was known that the intervention took place;
- for recommendations that were not implemented, the value of *u* was zero as no intervention took place; and
- for recommendations where it was unknown whether or not the recommendation was implemented, a *u* value of 0.818 was used in the baseline scenario based on the proportion of all DRPs that were resolved in the dataset (discussed in Section 5.4.6.1). This was necessary as it was inappropriate to consider that all interventions with unknown outcomes would have been implemented or not implemented. As there was some uncertainty regarding this *u* value, it was varied in the sensitivity analysis from the lowest rate reported in previous studies of HMRs (42%)[126] to 1.0 (the "best case", see Section 6.4.5).

As all of the recommendations made in HMR 11 were implemented, the *total outcomes* calculated in Step 3 (Table 160) were multiplied by a *u* of 1.0, and were therefore unchanged.

Step 5 - Attribution of proportions of the* total outcomes *to either the HMR or usual care

At this point in the calculation, the experts' estimates of *attribution* (*a*, the likelihood of another person involved in the patients' care undertaking the same intervention) were used to attribute proportions of the *total outcomes* to either the HMR or usual care. The *total outcomes* were multiplied by *a* to calculate the proportion of the *total outcomes* attributed to the HMR, and (1- *a*) for the proportion attributed to usual care.

The results of this calculation for HMR 11 are shown in Table 161.

TABLE 161 - ATTRIBUTED *TOTAL OUTCOMES* FOR HMR 111

DRP	MEAN OF ATTRIBUTION ESTIMATES FOR DRP	PARAMETER	TOTAL OF ESTIMATED CHANGE	ATTRIBUTED ESTIMATED CHANGE	
				HMR	USUAL CARE
53	60.7	Days of ill health	1.6	1.0	0.6
		Number (cost, $) of GP visits	0.5 (14.77)	0.3 (8.97)	0.2 (5.80)
		Number (cost, $) of specialist visits	0.1 (7.52)	0.1 (4.56)	0.0 (2.96)
		Cost of laboratory/ pathology tests ($)	11.4	6.92	4.48
		Duration (cost, $) of hospitalisation	0.2 (147.09)	0.1 (89.28)	0.1 (57.81)
		QOL lost (QALY)	-0.002	-0.001	-0.001
		Drug costs	140.40	85.22	55.18
54	64.1	Days of ill health	0.3	0.2	0.1
		Number (cost, $) of GP visits	0 (3.19)	0.0 (2.04)	0.0 (1.15)
		Number (cost, $) of specialist visits	0 (0.83)	0.0 (0.53)	0.0 (0.30)
		Cost of laboratory/ pathology tests ($)	3.7	2.37	1.33
		Duration (cost, $) of hospitalisation	0 (17.72)	0.0 (11.36)	0.0 (6.36)
		QOL lost (QALY)	0.000	0.000	0.000
55	50.8	Days of ill health	2.5	1.3	1.2
		Number (cost, $) of GP visits	0.6 (17.82)	0.3 (9.05)	0.3 (8.77)
		Number (cost, $) of specialist visits	0.2 (11.21)	0.1 (5.69)	0.1 (5.52)
		Cost of laboratory/ pathology tests ($)	11	5.59	5.41
		Duration (cost, $) of hospitalisation	0.1 (103.67)	0.1 (52.66)	0.0 (51.01)
		QOL lost (QALY)	-0.006	-0.003	-0.003
Totals		Days of ill health	4.4	2.4	2.0
		Number (cost, $) of GP visits	1.1 (35.78)	0.6 (20.06)	0.49 (15.71)
		Number (cost, $) of specialist visits	0.3 (19.56)	0.2 (10.79)	0.1 (8.77)
		Cost of laboratory/ pathology tests ($)	26.10	14.88	11.22
		Duration (cost, $) of hospitalisation	0.3 (268.48)	0.2 (153.31)	0.1 (115.17)
		QOL lost (QALY)	-0.008	-0.004	-0.004
		Drug costs	140.40	85.22	55.18

As there was considerable uncertainty regarding the values of *a* for every DRP, each was represented by an appropriate distribution for PSA in the cost-utility analysis calculations (Section 6.4). An additional scenario analysis was undertaken whereby *a*

was assigned a value of 1.0, for comparison to previous studies of HMRs that used expert opinion to estimate their cost-effectiveness (Section 6.4.4).[86, 139]

Step 6 - Final calculation of QOL and costs

To calculate the final estimate for each parameter with and without the HMR, the attributed *total outcomes* for both the HMR and usual care scenarios (calculated in Step 5) were subtracted from the estimates of QOL and healthcare costs that would have occurred in the absence of any intervention (calculated in Step 2).

These values for HMR 11 are shown in Table 162.

TABLE 162 - FINAL ESTIMATES OF QOL AND HEALTH RESOURCE UTILISATION THAT OCCURRED WITH- AND WITHOUT THE HMR IN HMR 11

PARAMETER	BEFORE	AFTER	
		WITH HMR	WITHOUT HMR
Days of ill health	6.9	4.5	4.9
Number (cost, $) of GP visits	2.0 (68.11)	1.4 (48.05)	1.5 (52.39)
Number (cost, $) of specialist visits	0.5 (32.28)	0.3 (21.49)	0.4 (23.51)
Cost of laboratory/ pathology tests ($)	51.00	36.12	39.78
Duration (cost, $) of hospitalisation	0.4 (419.54)	0.2 (266.23)	0.3 (304.37)
QOL (QALY)	0.986	0.990	0.990
Drug costs	2764.56	2679.34	2709.38
HMR cost	-	323.80	-
Total costs	3335.49	3375.03	3129.43

Calculation of potential clinical outcomes

The calculation of the estimated clinical outcomes for each HMR, expressed in terms of the estimated probability of the consequences they prevented and incurred (See Section 6.3.4.1), was essentially a simplified methodology of the calculations shown above. As no costs or QOL measures were estimated, only the experts' estimates of the consequences and their before- and after-intervention probabilities were required, and the consequences table was not used.

The experts' estimates of the probabilities of the consequences before and after the intervention were initially used to calculate estimates of baseline consequence probabilities and total probability changes. Similarly to the costs and QOL effect calculations, the total probability changes were then multiplied by the uptake parameter. Then, the attribution estimates were used to assign appropriate proportions of the probability changes to either the HMR or usual care scenarios to generate final estimates of the profanities of the consequences occurring with and without the HMR.

Appendix XXII - Supplementary HMR costing data

TABLE 163 - BASELINE SCENARIO - ESTIMATED QOL AND RESOURCE UTILISATION WITHOUT HMR IN DATASET OF 60 COMMON HMRS

HMR	QOL LOST (QALY)	ANNUAL DRUG COSTS ($)	DAYS OF ILL HEALTH	NUMBER (COST, $) OF GP VISITS	NUMBER (COST, $) OF SPECIALIST VISITS	DAYS IN HOSPITAL	COST OF HOSPITALISATION ($)	COST OF PATHOLOGY INVESTIGATIONS ($)	TOTAL COSTS ($)
3	0.042	2842.40	16.4	4.1 (133.09)	0.9 (49.89)	1.2	1336.51	221.16	4583.06
11	0.010	2719.75	5.0	2.6 (102.27)	0.4 (23.69)	0.3	310.20	39.35	3195.26
21	0.004	1323.91	3.4	2.6 (97.43)	0.3 (15.10)	0.3	234.77	51.47	1722.69
26	0.047	486.07	22.3	8.3 (285.12)	0.8 (46.06)	1.2	1018.00	218.49	2053.75
34	0.024	2652.96	15.1	9.8 (216.58)	0.9 (55.30)	0.5	510.38	144.98	3580.21
35	0.032	2827.16	20.9	15.3 (524.40)	1.8 (112.12)	1.5	1500.58	270.95	5235.21
36	0.016	2435.04	7.8	5.0 (181.86)	0.1 (4.62)	0.1	165.76	0.15	2787.43
49	0.001	2258.91	3.0	1.9 (29.90)	0.1 (4.88)	0.0	37.22	17.84	2348.74
51	0.012	1513.55	6.1	3.9 (120.14)	0.4 (21.33)	0.2	141.74	64.90	1861.66
54	0.009	1296.58	5.3	5.8 (199.77)	0.2 (14.03)	0.3	296.55	70.57	1877.50
56	0.033	1826.86	16.8	12.7 (369.45)	0.6 (38.18)	0.9	780.41	169.15	3184.06
69	0.011	2940.04	5.4	4.3 (166.92)	0.5 (28.21)	0.5	439.77	70.11	3645.06
76	0.013	5180.77	5.7	4.3 (164.91)	0.4 (27.32)	0.6	541.35	136.06	6050.41
80	0.012	3158.21	7.8	6.6 (245.80)	0.4 (21.32)	0.3	367.64	83.35	3876.32
81	0.001	5711.08	0.7	1.3 (51.35)	0.1 (6.09)	0.0	49.17	21.45	5839.14
83	0.011	806.17	7.7	7.7 (223.15)	0.2 (13.09)	0.1	223.01	24.28	1289.70

HMR	QOL LOST (QALY)	ANNUAL DRUG COSTS ($)	DAYS OF ILL HEALTH	NUMBER (COST, $) OF GP VISITS	NUMBER (COST, $) OF SPECIALIST VISITS	DAYS IN HOSPITAL	COST OF HOSPITALISATION ($)	COST OF PATHOLOGY INVESTIGATIONS ($)	TOTAL COSTS ($)
106	0.083	2656.62	34.1	12.6 (401.33)	1.1 (63.08)	1.6	1208.74	190.15	4519.91
113	0.014	2404.03	6.7	11.5 (448.49)	0.3 (15.50)	0.4	366.89	140.67	3375.57
121	0.037	1265.70	19.4	13.4 (255.63)	0.9 (55.35)	0.5	469.34	143.43	2189.45
127	0.011	3266.21	4.7	2.7 (85.59)	0.4 (23.60)	0.3	364.91	74.69	3815.00
129	0.013	1393.03	7.3	6.0 (132.11)	0.4 (25.06)	0.2	255.48	75.21	1880.90
147	0.011	3346.27	6.3	5.0 (186.97)	0.3 (17.73)	0.3	303.64	96.71	3951.31
148	0.013	1160.34	13.7	6.8 (150.46)	0.3 (18.12)	0.2	302.05	35.76	1666.73
164	0.015	4916.12	9.0	9.3 (338.09)	0.4 (23.23)	0.5	441.86	147.73	5867.03
200	0.006	2032.46	4.1	5.9 (228.66)	0.1 (7.14)	0.2	275.12	52.75	2596.12
225	0.009	1697.39	4.0	3.8 (120.19)	0.2 (12.00)	0.2	155.37	42.79	2027.75
227	0.001	2842.22	5.3	3.1 (44.42)	0.1 (6.31)	0.0	31.32	24.79	2949.07
229	0.005	3978.11	3.4	2.6 (55.08)	0.1 (6.77)	0.1	65.29	36.23	4141.48
268	0.002	5866.86	1.5	1.6 (58.16)	0.0 (2.65)	0.1	61.03	14.36	6003.06
271	0.008	1775.97	4.1	6.2 (239.51)	0.4 (21.05)	0.3	333.42	118.60	2488.54
285	0.009	2257.86	4.6	4.9 (165.17)	0.2 (10.71)	0.1	125.02	41.25	2600.00
289	0.000	4080.78	0.3	0.7 (27.10)	0.1 (3.29)	0.0	35.09	4.33	4150.59
295	0.005	1173.32	3.7	3.1 (110.80)	0.3 (18.89)	0.4	373.84	79.61	1756.46
313	0.015	9621.90	17.2	14.7 (304.75)	0.3 (20.40)	0.3	336.73	117.99	10401.77
315	0.004	997.33	3.7	2.8 (109.52)	0.1 (9.66)	0.1	141.49	34.54	1292.53
326	0.003	3549.14	3.2	2.8 (85.47)	0.1 (8.13)	0.1	135.28	32.67	3810.68

HMR	QOL LOST (QALY)	ANNUAL DRUG COSTS ($)	DAYS OF ILL HEALTH	NUMBER (COST, $) OF GP VISITS	NUMBER (COST, $) OF SPECIALIST VISITS	DAYS IN HOSPITAL	COST OF HOSPITALISATION ($)	COST OF PATHOLOGY INVESTIGATIONS ($)	TOTAL COSTS ($)
332	0.007	5936.73	4.9	4.3 (143.91)	0.4 (27.54)	0.3	344.96	112.40	6565.55
336	0.021	2311.85	10.2	8.2 (304.77)	0.5 (31.00)	0.7	657.74	191.67	3497.02
352	0.008	24731.83	3.8	1.8 (70.51)	0.3 (15.56)	0.2	230.66	26.82	25075.39
355	0.005	2837.74	6.3	5.2 (138.58)	0.2 (10.64)	0.1	68.28	27.22	3082.46
370	0.003	2149.74	1.7	2.0 (76.87)	0.0 (1.58)	0.0	37.69	17.71	2283.59
382	0.014	6897.95	9.5	6.2 (235.20)	0.2 (13.71)	0.1	118.50	62.86	7328.23
392	0.005	4125.68	2.4	3.0 (97.02)	0.3 (18.50)	0.2	193.29	60.81	4495.31
394	0.006	2502.93	6.2	3.6 (92.07)	0.2 (12.85)	0.3	316.04	62.59	2986.48
395	0.004	3969.28	2.8	3.7 (136.69)	0.1 (5.08)	0.2	144.80	39.88	4295.74
418	0.003	2593.98	5.9	6.4 (122.86)	0.2 (9.47)	0.1	60.98	53.15	2840.45
434	0.016	4165.68	13.7	9.1 (189.41)	0.2 (12.62)	0.2	267.82	34.10	4669.63
446	0.010	2515.24	15.2	12.3 (243.95)	0.2 (12.59)	0.1	139.23	54.09	2965.11
467	0.001	6403.18	0.4	0.9 (33.74)	0.0 (3.26)	0.0	28.87	8.10	6477.15
478	0.003	261.28	1.9	3.3 (111.68)	0.1 (4.69)	0.0	37.99	23.60	439.24
479	0.018	509.17	7.7	5.1 (148.43)	0.7 (40.23)	0.4	454.12	129.07	1281.02
484	0.002	4046.71	1.3	2.8 (110.08)	0.0 (2.05)	0.1	67.02	31.45	4257.30
487	0.031	1679.70	24.7	14.0 (185.87)	0.8 (49.15)	0.3	236.16	132.11	2282.99
517	0.005	11539.85	3.5	5.1 (158.51)	0.2 (13.39)	0.1	120.51	52.85	11885.12
569	0.004	2689.31	2.6	3.2 (117.21)	0.1 (7.74)	0.1	113.35	34.35	2961.96
619	0.003	3711.42	2.2	3.4 (104.76)	0.1 (6.52)	0.0	29.91	36.08	3888.69

HMR	QOL LOST (QALY)	ANNUAL DRUG COSTS ($)	DAYS OF ILL HEALTH	NUMBER (COST, $) OF GP VISITS	NUMBER (COST, $) OF SPECIALIST VISITS	DAYS IN HOSPITAL	COST OF HOSPITALISATION ($)	COST OF PATHOLOGY INVESTIGATIONS ($)	TOTAL COSTS ($)
626	0.003	1948.16	13.4	11.0 (195.57)	0.3 (20.21)	0.2	149.47	86.29	2399.70
660	0.004	2424.65	2.6	2.8 (114.39)	0.3 (15.15)	0.3	300.30	50.04	2904.52
666	0.020	1525.18	10.2	7.4 (212.47)	0.9 (55.30)	0.7	690.20	211.74	2694.89
674	0.014	2592.94	22.4	13.8 (267.79)	0.6 (41.93)	0.5	421.24	141.29	3465.18
TOTAL	**0.753**	**204331.28**	**481.2**	**354.4 (10271.98)**	**21.3 (1280.68)**	**19.3**	**18964.08**	**4788.83**	**239636.85**

TABLE 164 - BASELINE SCENARIO - ESTIMATED QOL AND RESOURCE UTILISATION WITH HMR IN DATASET OF 60 COMMON HMRS

HMR	QOL LOST (QALY)	ANNUAL DRUG COSTS ($)	DAYS OF ILL HEALTH	NUMBER (COST, $) OF GP VISITS	NUMBER (COST, $) OF SPECIALIST VISITS	DAYS IN HOSPITAL	COST OF HOSPITALISATION ($)	COST OF PATHOLOGY INVESTIGATIONS ($)	HMR COST ($)	TOTAL COSTS ($)
3	0.031	3100.93	12.47852	4.1 (134.78)	0.7 (41.49)	0.9	995.79	178.14	323.80	4774.93
11	0.005	2634.56	2.57635	1.9 (71.54)	0.2 (12.84)	0.2	154.22	24.63	323.80	3221.60
21	0.004	1594.94	2.82613	3.0 (115.50)	0.3 (18.09)	0.3	280.08	46.17	323.80	2378.58
26	0.045	287.24	21.09516	8.5 (291.72)	0.7 (44.31)	1.1	956.96	207.75	323.80	2111.78
34	0.019	2652.96	12.29378	8.8 (215.68)	0.8 (50.03)	0.5	494.15	132.38	323.80	3869.00
35	0.030	2827.16	17.61925	12.0 (430.23)	1.4 (89.21)	1.3	1285.11	231.71	323.80	5187.22
36	0.012	2435.04	5.84339	4.5 (163.72)	0.1 (3.48)	0.1	122.57	0.21	323.80	3048.81
49	0.001	2069.05	2.40416	1.6 (24.58)	0.1 (3.82)	0.0	30.65	14.28	323.80	2466.19
51	0.008	1513.55	4.55355	3.2 (98.69)	0.3 (15.10)	0.1	95.49	48.50	323.80	2095.14
54	0.008	1290.58	4.69833	5.2 (173.16)	0.2 (12.20)	0.3	260.84	60.47	323.80	2121.06
56	0.035	1544.95	17.21536	12.5 (364.36)	0.6 (38.47)	0.9	801.13	166.01	323.80	3238.72
69	0.010	2764.88	4.96130	3.5 (133.02)	0.5 (28.35)	0.5	443.69	62.08	323.80	3755.81
76	0.012	5176.57	5.46738	4.3 (162.05)	0.4 (24.07)	0.6	548.03	125.74	323.80	6360.26
80	0.011	3128.17	7.05481	5.5 (207.25)	0.4 (20.91)	0.3	322.12	66.60	323.80	4068.86
81	0.001	5712.44	0.51444	1.0 (36.65)	0.1 (4.16)	0.0	34.32	13.68	323.80	6125.04
83	0.010	861.42	6.50858	6.4 (185.52)	0.2 (11.82)	0.1	204.57	20.55	323.80	1607.68
106	0.077	2656.62	31.82626	12.2 (391.72)	1.1 (60.90)	1.5	1142.00	179.06	323.80	4754.10
113	0.014	2392.45	6.90830	10.7 (416.37)	0.3 (15.25)	0.4	365.38	127.05	323.80	3640.30
121	0.037	1227.39	18.95005	12.9 (241.69)	0.9 (53.74)	0.5	483.28	142.33	323.80	2472.23

HMR	QOL LOST (QALY)	ANNUAL DRUG COSTS ($)	DAYS OF ILL HEALTH	NUMBER (COST, $) OF GP VISITS	NUMBER (COST, $) OF SPECIALIST VISITS	DAYS IN HOSPITAL	COST OF HOSPITALISATION ($)	COST OF PATHOLOGY INVESTIGATIONS ($)	HMR COST ($)	TOTAL COSTS ($)
127	0.010	3266.21	4.29248	2.6 (82.13)	0.4 (21.78)	0.3	324.71	68.78	323.80	4087.42
129	0.012	1527.63	6.86008	5.7 (124.32)	0.4 (22.75)	0.2	210.32	63.89	323.80	2272.70
147	0.010	3334.01	6.26931	4.4 (166.45)	0.3 (17.64)	0.3	276.76	79.45	323.80	4198.11
148	0.010	1160.34	11.26967	5.9 (123.93)	0.3 (14.56)	0.2	230.91	31.88	323.80	1885.41
164	0.013	4933.30	7.47712	8.2 (296.87)	0.4 (22.62)	0.4	401.12	123.48	323.80	6101.18
200	0.006	2054.35	3.80916	5.4 (210.14)	0.1 (6.45)	0.2	289.88	47.96	323.80	2932.59
225	0.010	1697.39	4.18175	3.5 (109.53)	0.2 (11.80)	0.2	168.80	42.46	323.80	2353.80
227	0.001	2635.92	5.28966	3.1 (44.65)	0.1 (6.25)	0.0	31.64	24.88	323.80	3067.14
229	0.004	3694.58	2.69539	2.1 (43.30)	0.1 (5.94)	0.1	58.12	28.52	323.80	4154.27
268	0.002	6311.49	1.38562	1.4 (50.24)	0.0 (2.47)	0.1	60.15	12.89	323.80	6761.04
271	0.007	1972.33	3.74121	6.0 (228.44)	0.3 (19.52)	0.3	310.01	109.26	323.80	2963.36
285	0.009	2235.22	4.70205	4.9 (165.37)	0.2 (10.99)	0.1	121.70	41.49	323.80	2898.55
289	0.000	4080.78	0.24462	0.6 (25.80)	0.0 (2.71)	0.0	24.28	3.91	323.80	4461.28
295	0.005	1173.32	3.70910	3.1 (108.39)	0.3 (18.52)	0.4	375.68	79.29	323.80	2078.99
313	0.013	9621.90	16.40109	14.0 (279.39)	0.3 (19.31)	0.3	301.17	116.67	323.80	10662.25
315	0.004	772.66	3.06058	2.7 (103.41)	0.1 (8.28)	0.1	138.58	32.68	323.80	1379.40
326	0.002	3549.14	2.58542	2.3 (68.78)	0.1 (6.69)	0.1	113.45	26.74	323.80	4088.60
332	0.005	5589.37	3.35704	2.7 (88.61)	0.3 (19.42)	0.2	234.56	76.21	323.80	6331.98
336	0.019	2301.41	9.20657	8.2 (302.53)	0.5 (30.91)	0.6	620.46	187.47	323.80	3766.57
352	0.010	24731.83	4.72953	1.4 (54.21)	0.3 (17.40)	0.2	263.98	17.62	323.80	25408.84

HMR	QOL LOST (QALY)	ANNUAL DRUG COSTS ($)	DAYS OF ILL HEALTH	NUMBER (COST, $) OF GP VISITS	NUMBER (COST, $) OF SPECIALIST VISITS	DAYS IN HOSPITAL	COST OF HOSPITALISATION ($)	COST OF PATHOLOGY INVESTIGATIONS ($)	HMR COST ($)	TOTAL COSTS ($)
355	0.004	2837.74	5.17163	4.8 (125.00)	0.1 (6.51)	0.0	35.89	21.14	323.80	3350.08
370	0.002	2149.74	1.48044	1.7 (68.65)	0.0 (1.37)	0.0	32.83	15.38	323.80	2591.78
382	0.010	7182.92	6.81893	5.6 (213.65)	0.2 (11.20)	0.1	112.52	59.26	323.80	7903.34
392	0.003	4144.53	1.60215	2.4 (76.63)	0.2 (11.71)	0.1	121.18	37.04	323.80	4714.88
394	0.004	2244.60	3.92047	3.0 (85.87)	0.2 (12.16)	0.2	195.96	47.42	323.80	2909.80
395	0.006	3940.76	3.32986	3.8 (134.19)	0.1 (6.72)	0.2	151.34	41.92	323.80	4598.73
418	0.003	2593.98	5.44478	5.8 (113.00)	0.2 (9.07)	0.1	64.82	47.96	323.80	3152.64
434	0.014	4165.68	12.21234	8.5 (172.30)	0.2 (11.28)	0.1	238.09	32.02	323.80	4943.17
446	0.008	2515.24	13.40565	11.2 (213.57)	0.2 (10.71)	0.1	117.47	49.49	323.80	3230.29
467	0.001	6381.14	0.45500	0.7 (27.97)	0.0 (2.50)	0.0	28.61	6.09	323.80	6770.11
478	0.003	261.28	1.61181	3.1 (107.48)	0.1 (3.31)	0.0	34.71	20.07	323.80	750.65
479	0.011	512.58	4.99760	4.2 (129.41)	0.4 (26.12)	0.3	348.68	100.75	323.80	1441.34
484	0.002	4010.50	1.14097	2.6 (103.92)	0.0 (2.67)	0.1	64.66	30.08	323.80	4535.63
487	0.032	1698.24	22.82809	13.0 (181.46)	0.8 (46.16)	0.3	266.28	124.31	323.80	2640.25
517	0.004	11349.45	3.47121	4.3 (134.51)	0.2 (10.67)	0.1	118.68	51.42	323.80	11988.54
569	0.005	2639.34	2.78978	3.2 (115.13)	0.1 (6.76)	0.1	108.90	30.83	323.80	3224.76
619	0.003	3711.42	2.12779	3.1 (95.62)	0.1 (6.16)	0.0	28.19	34.77	323.80	4199.96
626	0.003	1443.99	14.26678	11.1 (189.21)	0.3 (20.91)	0.2	142.74	83.78	323.80	2204.44
660	0.003	2339.48	2.11403	2.3 (93.81)	0.2 (11.77)	0.2	241.97	37.71	323.80	3048.55
666	0.018	1536.16	9.82619	7.4 (208.76)	0.9 (52.78)	0.6	635.82	202.71	323.80	2960.03

HMR	QOL LOST (QALY)	ANNUAL DRUG COSTS ($)	DAYS OF ILL HEALTH	NUMBER (COST, $) OF GP VISITS	NUMBER (COST, $) OF SPECIALIST VISITS	DAYS IN HOSPITAL	COST OF HOSPITALISATION ($)	COST OF PATHOLOGY INVESTIGATIONS ($)	HMR COST ($)	TOTAL COSTS ($)
674	0.011	2592.94	19.56833	12.2 (227.40)	0.5 (33.57)	0.3	312.46	117.38	323.80	3607.54
Total	**0.673**	**202765.78**	**429.64634**	**324.0 (9352.25)**	**18.9 (1138.37)**	**17.4**	**16978.46**	**4254.44**	**19428.00**	**253917.28**

TABLE 165 - BASELINE SCENARIO - ESTIMATED QOL AND RESOURCE UTILISATION WITHOUT ANY INTERVENTION (HMR OR OTHERWISE) IN DATASET OF 60 COMMON HMRS

HMR	QOL LOST (QALY)	ANNUAL DRUG COSTS ($)	DAYS OF ILL HEALTH	NUMBER (COST, $) OF GP VISITS	NUMBER (COST, $) OF SPECIALIST VISITS	DAYS IN HOSPITAL	COST OF HOSPITALISATION ($)	COST OF PATHOLOGY INVESTIGATIONS ($)	TOTAL COSTS ($)
3	0.053	2 543.83	20.4	4.1 (131.44)	1.0 (59.11)	1.6	1 689.44	265.71	4 689.53
11	0.014	2 774.96	7.0	3.2 (125.12)	0.6 (32.49)	0.4	426.93	50.49	3 410.00
21	0.005	1 149.12	3.8	2.3 (86.33)	0.2 (13.19)	0.2	206.20	55.82	1 510.67
26	0.049	566.08	23.4	8.2 (280.57)	0.8 (47.56)	1.3	1 068.19	226.11	2 188.51
34	0.028	2 652.96	17.4	10.5 (213.04)	0.9 (58.97)	0.5	517.17	154.56	3 596.71
35	0.033	2 827.16	23.4	17.6 (603.21)	2.1 (133.85)	1.7	1 695.75	302.27	5 562.23
36	0.020	2 435.04	9.9	5.5 (201.08)	0.1 (5.82)	0.1	211.35	0.09	2 853.39
49	0.001	2 392.68	3.3	2.1 (32.31)	0.1 (5.35)	0.0	40.19	19.45	2 489.98
51	0.014	1 513.55	6.9	4.2 (131.26)	0.5 (24.51)	0.2	163.85	73.13	1 906.31
54	0.009	1 299.82	5.8	6.2 (219.86)	0.3 (15.06)	0.3	320.38	78.58	1 933.70
56	0.032	2 081.95	16.3	12.9 (374.35)	0.6 (37.90)	0.8	760.45	172.18	3 426.83
69	0.012	3 025.20	5.7	4.8 (185.42)	0.5 (28.40)	0.5	446.10	76.08	3 761.20
76	0.014	5 180.79	5.9	4.3 (165.48)	0.5 (30.41)	0.6	541.85	145.85	6 064.39
80	0.012	3 187.81	8.3	7.5 (274.99)	0.4 (21.72)	0.3	401.95	97.11	3 983.59
81	0.002	5 709.82	0.8	1.6 (60.76)	0.1 (7.32)	0.0	58.85	26.26	5 863.02
83	0.014	726.90	9.1	9.0 (267.07)	0.3 (14.80)	0.2	248.09	28.29	1 285.15
106	0.095	2 656.62	38.7	13.4 (420.77)	1.2 (67.48)	1.8	1 343.78	212.59	4 701.25
113	0.014	2 411.95	6.6	12.1 (470.65)	0.3 (15.66)	0.4	368.46	149.83	3 416.55
121	0.037	1 316.92	20.0	14.0 (272.25)	0.9 (57.43)	0.5	451.39	144.91	2 242.89

HMR	QOL LOST (QALY)	ANNUAL DRUG COSTS ($)	DAYS OF ILL HEALTH	NUMBER (COST, $) OF GP VISITS	NUMBER (COST, $) OF SPECIALIST VISITS	DAYS IN HOSPITAL	COST OF HOSPITALISATION ($)	COST OF PATHOLOGY INVESTIGATIONS ($)	TOTAL COSTS ($)
127	0.012	3 266.21	5.7	3.0 (93.08)	0.4 (26.45)	0.4	449.49	86.43	3 921.67
129	0.013	1 236.39	7.5	6.0 (133.62)	0.4 (26.91)	0.2	291.13	81.99	1 770.03
147	0.011	3 357.59	6.3	5.7 (210.62)	0.3 (17.73)	0.4	334.48	116.53	4 036.95
148	0.016	1 160.34	15.8	7.6 (178.61)	0.4 (21.10)	0.3	368.05	38.64	1 766.75
164	0.017	4 894.50	10.2	10.5 (376.42)	0.4 (23.79)	0.5	483.19	175.56	5 953.46
200	0.007	2 014.80	4.3	6.4 (245.99)	0.1 (7.66)	0.2	256.98	57.17	2 582.60
225	0.008	1 697.39	3.8	4.1 (128.46)	0.2 (12.19)	0.2	144.14	42.91	2 025.10
227	0.001	3 031.56	5.4	3.1 (44.21)	0.1 (6.37)	0.0	31.03	24.71	3 137.89
229	0.006	4 275.74	4.1	3.1 (67.29)	0.1 (7.61)	0.1	72.82	44.24	4 467.70
268	0.003	5 602.03	1.6	1.9 (68.62)	0.1 (3.25)	0.1	61.74	16.41	5 752.04
271	0.010	1 470.55	4.6	6.7 (259.35)	0.4 (23.50)	0.4	368.66	133.99	2 256.05
285	0.009	2 277.94	4.6	4.8 (165.00)	0.2 (10.47)	0.1	127.86	41.05	2 622.31
289	0.001	4 080.78	0.3	0.7 (27.89)	0.1 (3.64)	0.1	41.68	4.59	4 158.58
295	0.005	1 173.32	3.7	3.2 (112.53)	0.4 (19.15)	0.4	372.53	79.85	1 757.37
313	0.016	9 621.90	17.7	15.1 (318.93)	0.3 (21.01)	0.3	356.60	118.73	10 437.17
315	0.005	1 168.30	4.1	2.9 (114.17)	0.2 (10.71)	0.1	143.70	35.96	1 472.83
326	0.004	3 549.14	3.7	3.1 (97.20)	0.2 (9.02)	0.1	147.57	36.31	3 839.25
332	0.009	6 120.85	6.0	5.4 (185.74)	0.5 (32.89)	0.3	421.48	137.97	6 898.93
336	0.023	2 322.85	11.5	8.2 (309.10)	0.5 (31.01)	0.7	698.70	196.51	3 558.16
352	0.007	24 731.83	3.3	2.0 (80.00)	0.3 (15.51)	0.2	216.25	34.01	25 077.60

HMR	QOL LOST (QALY)	ANNUAL DRUG COSTS ($)	DAYS OF ILL HEALTH	NUMBER (COST, $) OF GP VISITS	NUMBER (COST, $) OF SPECIALIST VISITS	DAYS IN HOSPITAL	COST OF HOSPITALISATION ($)	COST OF PATHOLOGY INVESTIGATIONS ($)	TOTAL COSTS ($)
355	0.005	2 837.74	7.3	5.6 (151.48)	0.2 (14.61)	0.1	100.76	32.84	3 137.42
370	0.003	2 149.74	1.9	2.1 (81.21)	0.0 (1.68)	0.1	40.24	18.94	2 291.81
382	0.016	6 716.46	11.2	6.6 (250.17)	0.2 (15.42)	0.1	123.09	65.32	7 170.46
392	0.006	4 109.78	3.1	3.6 (113.78)	0.4 (23.87)	0.2	250.92	79.84	4 578.19
394	0.008	2 753.38	8.4	4.1 (94.75)	0.2 (12.84)	0.5	430.04	76.89	3 367.90
395	0.003	3 985.88	2.5	3.7 (138.11)	0.1 (4.07)	0.1	140.63	38.69	4 307.38
418	0.003	2 593.98	6.2	6.9 (131.09)	0.2 (9.86)	0.0	58.43	57.34	2 850.70
434	0.017	4 165.68	14.8	9.6 (203.58)	0.2 (13.67)	0.2	292.91	35.52	4 711.37
446	0.013	2 515.24	17.2	13.5 (278.54)	0.2 (14.67)	0.1	163.52	59.12	3 031.08
467	0.001	6 413.35	0.4	0.9 (37.10)	0.1 (3.70)	0.0	29.02	9.27	6 492.44
478	0.004	261.28	2.2	3.4 (115.50)	0.1 (5.98)	0.0	41.56	26.91	451.23
479	0.023	505.80	10.0	5.8 (163.28)	0.9 (52.08)	0.5	544.56	153.19	1 418.91
484	0.003	4 098.34	1.7	3.0 (118.38)	0.0 (1.36)	0.1	72.73	34.03	4 324.84
487	0.031	1 654.62	26.7	15.3 (191.95)	0.8 (52.51)	0.2	195.01	141.10	2 235.19
517	0.005	11 725.95	3.4	5.6 (177.04)	0.3 (15.48)	0.2	120.09	52.19	12 090.76
569	0.004	2 725.50	2.4	3.3 (119.21)	0.1 (8.51)	0.1	116.88	37.48	3 007.57
619	0.003	3 711.42	2.3	3.6 (113.40)	0.1 (6.84)	0.0	31.44	37.25	3 900.35
626	0.003	2 220.15	13.2	11.0 (199.81)	0.3 (20.02)	0.2	152.69	88.74	2 681.41
660	0.005	2 505.08	3.1	3.3 (133.77)	0.3 (18.32)	0.4	354.89	61.56	3 073.62
666	0.022	1 512.40	10.5	7.5 (216.44)	0.9 (58.14)	0.7	749.92	221.71	2 758.61

HMR	QOL LOST (QALY)	ANNUAL DRUG COSTS ($)	DAYS OF ILL HEALTH	NUMBER (COST, $) OF GP VISITS	NUMBER (COST, $) OF SPECIALIST VISITS	DAYS IN HOSPITAL	COST OF HOSPITALISATION ($)	COST OF PATHOLOGY INVESTIGATIONS ($)	TOTAL COSTS ($)
674	0.017	2 592.94	25.0	15.2 (302.06)	0.8 (50.09)	0.6	527.84	163.73	3 636.66
TOTAL	**0.834**	**205 261.86**	**530.4**	**380.9 (11 063.42)**	**23.4 (1 410.73)**	**21.2**	**20 885.65**	**5 274.56**	**243 896.22**

TABLE 166 - BASELINE SCENARIO - ESTIMATED QOL AND RESOURCE UTILISATION ACCORDING TO DRP TYPES AND SUBTYPES WITHOUT HMR IN DATASET OF 60 COMMON HMRS. NUMBERS IN BRACKETS SHOW AVERAGE PER DRP TYPE OR SUBTYPE

DRP TYPE SUBTYPE	NUMBER (%) OF DRPS	QOL LOST (QALY)	ANNUAL DRUG COSTS ($)	DAYS OF ILL HEALTH	NUMBER OF GP VISITS	COST OF GP VISITS ($)	NUMBER OF SPECIALIST VISITS	COST OF SPECIALIST VISITS ($)	DAYS IN HOSPITAL	COST OF HOSPITALISATION ($)	COST OF PATHOLOGY INVESTIGATIONS ($)	TOTAL COSTS ($)
Drug selection	**49 (27.2)**	**0.192 (0.004)**	**-1327.13 (-27.08)**	**123.0 (2.5)**	**94.5 (1.9)**	**2842.17 (58.00)**	**6.8 (0.1)**	**407.87 (8.32)**	**5.5 (0.1)**	**5382.41 (109.85)**	**1309.32 (26.72)**	**8614.64 (175.81)**
Duplication	4 (2.2)	0.021 (0.005)	-20.08 (-5.02)	11.7 (2.9)	8.5 (2.1)	237.34 (59.33)	0.9 (0.2)	51.16 (12.79)	0.7 (0.2)	687.30 (171.83)	156.22 (39.06)	1111.94 (277.98)
Drug interaction	14 (7.8)	0.042 (0.003)	-131.80 (-9.41)	24.8 (1.8)	21.8 (1.6)	694.33 (49.60)	1.9 (0.1)	107.16 (7.65)	1.2 (0.1)	1134.90 (81.06)	315.42 (22.53)	2120.01 (151.43)
Unnecessary therapy/ no apparent current indication	13 (7.2)	0.031 (0.002)	-854.67 (-65.74)	23.0 (1.8)	18.4 (1.4)	511.05 (39.31)	0.6 (0.0)	43.68 (3.36)	0.5 (0.0)	422.29 (32.48)	176.24 (13.56)	298.59 (22.97)
Contraindications apparent	16 (8.9)	0.097 (0.006)	-311.34 (-19.46)	62.6 (3.9)	44.6 (2.8)	1357.54 (84.85)	3.3 (0.2)	201.91 (12.62)	3.0 (0.2)	3064.32 (191.52)	643.74 (40.23)	4956.17 (309.76)
Other drug selection problem	2 (1.1)	0.001 (0.001)	-9.24 (-4.62)	0.9 (0.4)	1.1 (0.5)	41.92 (20.96)	0.1 (0.0)	3.96 (1.98)	0.1 (0.0)	73.60 (36.80)	17.69 (8.85)	127.93 (63.96)
Over or underdose prescribed	**14 (7.8)**	**0.040 (0.003)**	**-235.20 (-16.80)**	**30.6 (2.2)**	**18.9 (1.4)**	**497.70 (35.55)**	**1.4 (0.1)**	**83.79 (5.98)**	**1.3 (0.1)**	**1189.27 (84.95)**	**260.29 (18.59)**	**1795.85 (128.27)**
Dose too high	12 (6.7)	0.018 (0.001)	-236.91 (-19.74)	12.3 (1.0)	9.6 (0.8)	309.47 (25.79)	1.0 (0.1)	59.08 (4.92)	0.7 (0.1)	695.64 (57.97)	145.90 (12.16)	973.18 (81.10)
Dose too low	2 (1.1)	0.023 (0.011)	1.71 (0.85)	18.3 (9.1)	9.3 (4.6)	188.23 (94.12)	0.4 (0.2)	24.71 (12.36)	0.6 (0.3)	493.63 (246.82)	114.39 (57.19)	822.67 (411.33)
Compliance	**30 (16.7)**	**0.044 (0.001)**	**-191.80 (-6.39)**	**38.4 (1.3)**	**30.8 (1.0)**	**817.26 (27.24)**	**1.0 (0.0)**	**59.45 (1.98)**	**0.9 (0.0)**	**923.13 (30.77)**	**279.12 (9.30)**	**1887.16 (62.91)**
Taking too little	21 (11.7)	0.026 (0.001)	-184.12 (-8.77)	24.8 (1.2)	19.6 (0.9)	464.53 (22.12)	0.7 (0.0)	43.78 (2.08)	0.6 (0.0)	615.97 (29.33)	205.18 (9.77)	1145.34 (54.54)
Difficulty using dosage form	4 (2.2)	0.015 (0.004)	0.00 (0.00)	8.6 (2.2)	6.8 (1.7)	257.18 (64.29)	0.1 (0.0)	4.44 (1.11)	0.1 (0.0)	160.15 (40.04)	23.25 (5.81)	445.03 (111.26)

Other compliance problem	5 (2.8)	0.003 (0.001)	-7.68 (-1.54)	5.0 (1.0)	4.3 (0.9)	95.56 (19.11)	0.2 (0.0)	11.22 (2.24)	0.1 (0.0)	147.00 (29.40)	50.69 (10.14)	296.79 (59.36)
Untreated indications	**44 (24.4)**	**0.365 (0.008)**	**851.63 (19.36)**	**221.7 (5.0)**	**146.3 (3.3)**	**3949.44 (89.76)**	**9.0 (0.2)**	**540.83 (12.29)**	**8.8 (0.2)**	**8627.53 (196.08)**	**2138.26 (48.60)**	**16107.68 (366.08)**
Condition not adequately treated	28 (15.6)	0.253 (0.009)	228.08 (8.15)	142.1 (5.1)	101.6 (3.6)	2871.14 (102.54)	5.5 (0.2)	324.74 (11.60)	5.0 (0.2)	4805.92 (171.64)	1269.42 (45.34)	9499.31 (339.26)
Therapy required	16 (8.9)	0.111 (0.007)	623.55 (38.97)	79.6 (5.0)	44.7 (2.8)	1078.30 (67.39)	3.5 (0.2)	216.09 (13.51)	3.8 (0.2)	3821.60 (238.85)	868.83 (54.30)	6608.38 (413.02)
Monitoring	**16 (8.9)**	**0.019 (0.001)**	**0.00 (0.00)**	**13.6 (0.8)**	**15.3 (1.0)**	**389.50 (24.34)**	**0.7 (0.0)**	**39.29 (2.46)**	**0.3 (0.0)**	**307.38 (19.21)**	**182.49 (11.41)**	**918.65 (57.42)**
Laboratory monitoring	15 (8.3)	0.018 (0.001)	0.00 (0.00)	13.0 (0.9)	14.8 (1.0)	372.38 (24.83)	0.7 (0.0)	39.25 (2.62)	0.2 (0.0)	302.37 (20.16)	167.78 (11.19)	881.77 (58.78)
Non-laboratory monitoring	1 (0.6)	0.000 (0.000)	0.00 (0.00)	0.6 (0.6)	0.5 (0.5)	17.12 (17.12)	0.0 (0.0)	0.04 (0.04)	0.0 (0.0)	5.00 (5.00)	14.71 (14.71)	36.88 (36.88)
Education or information	**4 (2.2)**	**0.039 (0.010)**	**0.00 (0.00)**	**19.8 (5.0)**	**9.2 (2.3)**	**332.06 (83.02)**	**0.8 (0.2)**	**46.61 (11.65)**	**0.8 (0.2)**	**771.81 (192.95)**	**124.01 (31.00)**	**1274.48 (318.62)**
Patient drug information request	1 (0.6)	0.003 (0.003)	0.00 (0.00)	1.3 (1.3)	2.1 (2.1)	80.39 (80.39)	0.0 (0.0)	1.56 (1.56)	0.1 (0.1)	122.47 (122.47)	21.88 (21.88)	226.30 (226.30)
Confusion about therapy	1 (0.6)	0.001 (0.001)	0.00 (0.00)	1.4 (1.4)	1.1 (1.1)	26.43 (26.43)	0.0 (0.0)	1.40 (1.40)	0.0 (0.0)	20.98 (20.98)	6.04 (6.04)	54.84 (54.84)
Demonstration of device	2 (1.1)	0.035 (0.018)	0.00 (0.00)	17.1 (8.5)	6.0 (3.0)	225.24 (112.62)	0.7 (0.4)	43.65 (21.82)	0.7 (0.3)	628.36 (314.18)	96.10 (48.05)	993.34 (496.67)
Non-clinical	**1 (0.6)**	**0.001 (0.001)**	**0.00 (0.00)**	**0.7 (0.7)**	**1.7 (1.7)**	**64.70 (64.70)**	**0.0 (0.0)**	**1.92 (1.92)**	**0.0 (0.0)**	**46.35 (46.35)**	**12.40 (12.40)**	**125.38 (125.38)**
Dietary problem	1 (0.6)	0.001 (0.001)	0.00 (0.00)	0.7 (0.7)	1.7 (1.7)	64.70 (64.70)	0.0 (0.0)	1.92 (1.92)	0.0 (0.0)	46.35 (46.35)	12.40 (12.40)	125.38 (125.38)
Toxicity or adverse reaction	**22 (12.2)**	**0.053 (0.002)**	**-28.09 (-1.28)**	**33.3 (1.5)**	**37.7 (1.7)**	**1379.15 (62.69)**	**1.6 (0.1)**	**100.93 (4.59)**	**1.7 (0.1)**	**1716.20 (78.01)**	**482.95 (21.95)**	**3651.15 (165.96)**
Toxicity caused by dose	3 (1.7)	0.004 (0.001)	-222.61 (-74.20)	4.4 (1.5)	5.9 (2.0)	232.17 (77.39)	0.2 (0.1)	9.08 (3.03)	0.2 (0.1)	184.71 (61.57)	83.02 (27.67)	286.38 (95.46)
Toxicity caused by drug interaction	3 (1.7)	0.002 (0.001)	215.29 (71.76)	2.6 (0.9)	3.1 (1.0)	116.98 (38.99)	0.0 (0.0)	3.20 (1.07)	0.1 (0.0)	106.17 (35.39)	36.05 (12.02)	477.69 (159.23)

Toxicity evident	14 (7.8)	0.046 (0.003)	-322.16 (-23.01)	26.2 (1.9)	28.4 (2.0)	1016.46 (72.60)	1.4 (0.1)	88.02 (6.29)	1.5 (0.1)	1411.98 (100.86)	356.07 (25.43)	2550.38 (182.17)
Other toxicity/adverse effect problem	2 (1.1)	0.000 (0.000)	301.39 (150.70)	0.1 (0.1)	0.3 (0.2)	13.54 (6.77)	0.0 (0.0)	0.63 (0.32)	0.0 (0.0)	13.33 (6.67)	7.81 (3.91)	336.71 (168.35)
Total	**180 (100.0)**	**0.753 (0.004)**	**-930.58 (-5.17)**	**481.2 (2.7)**	**354.4 (2.0)**	**10271.98 (57.07)**	**21.3 (0.1)**	**1280.68 (7.11)**	**19.3 (0.1)**	**18964.08 (105.36)**	**4788.83 (26.60)**	**34374.99 (190.97)**

TABLE 167 - BASELINE SCENARIO - ESTIMATED QOL AND RESOURCE UTILISATION ACCORDING TO DRP TYPES AND SUBTYPES WITH HMR IN DATASET OF 60 COMMON HMRS. NUMBERS IN BRACKETS SHOW AVERAGE PER DRP TYPE OR SUBTYPE

DRP TYPE SUBTYPE	NUMBER (%) OF DRPS	QOL LOST (QALY)	ANNUAL DRUG COSTS ($)	DAYS OF ILL HEALTH	NUMBER OF GP VISITS	COST OF GP VISITS ($)	NUMBER OF SPECIALIST VISITS	COST OF SPECIALIST VISITS ($)	DAYS IN HOSPITAL	COST OF HOSPITALISATION ($)	COST OF PATHOLOGY INVESTIGATIONS ($)	TOTAL COSTS ($)
Drug selection	**49 (27.2)**	**0.171 (0.003)**	**-1669.49 (-34.07)**	**110.0 (2.2)**	**84.7 (1.7)**	**2548.66 (52.01)**	**5.7 (0.1)**	**344.90 (7.04)**	**4.9 (0.1)**	**4776.94 (97.49)**	**1095.98 (22.37)**	**7096.99 (144.84)**
Duplication	4 (2.2)	0.022 (0.006)	-22.64 (-5.66)	11.9 (3.0)	8.3 (2.1)	218.29 (54.57)	0.8 (0.2)	45.24 (11.31)	0.6 (0.2)	638.18 (159.55)	138.61 (34.65)	1017.68 (254.42)
Drug interaction	14 (7.8)	0.028 (0.002)	-152.00 (-10.86)	18.0 (1.3)	17.7 (1.3)	570.13 (40.72)	1.3 (0.1)	71.44 (5.10)	0.9 (0.1)	905.63 (64.69)	230.43 (16.46)	1625.64 (116.12)
Unnecessary therapy/ no apparent current indication	13 (7.2)	0.033 (0.003)	-1051.66 (-80.90)	23.7 (1.8)	17.4 (1.3)	474.04 (36.46)	0.6 (0.0)	41.47 (3.19)	0.6 (0.0)	453.19 (34.86)	170.12 (13.09)	87.17 (6.71)
Contraindications apparent	16 (8.9)	0.085 (0.005)	-425.78 (-26.61)	55.3 (3.5)	40.0 (2.5)	1234.15 (77.13)	3.0 (0.2)	181.47 (11.34)	2.6 (0.2)	2686.59 (167.91)	534.65 (33.42)	4211.07 (263.19)
Other drug selection problem	2 (1.1)	0.002 (0.001)	-17.40 (-8.70)	1.1 (0.5)	1.3 (0.7)	52.05 (26.02)	0.1 (0.0)	5.28 (2.64)	0.1 (0.0)	93.35 (46.67)	22.17 (11.09)	155.44 (77.72)
Over or underdose prescribed	**14 (7.8)**	**0.035 (0.002)**	**-394.81 (-28.20)**	**26.8 (1.9)**	**17.1 (1.2)**	**440.40 (31.46)**	**1.2 (0.1)**	**74.32 (5.31)**	**1.2 (0.1)**	**1037.94 (74.14)**	**235.28 (16.81)**	**1393.14 (99.51)**
Dose too high	12 (6.7)	0.015 (0.001)	-396.73 (-33.06)	10.2 (0.8)	8.0 (0.7)	253.62 (21.13)	0.9 (0.1)	51.58 (4.30)	0.6 (0.1)	584.79 (48.73)	125.94 (10.50)	619.20 (51.60)
Dose too low	2 (1.1)	0.020 (0.010)	1.92 (0.96)	16.6 (8.3)	9.0 (4.5)	186.78 (93.39)	0.3 (0.2)	22.74 (11.37)	0.5 (0.3)	453.15 (226.57)	109.34 (54.67)	773.94 (386.97)
Compliance	**30 (16.7)**	**0.037 (0.001)**	**-366.55 (-12.22)**	**33.1 (1.1)**	**26.9 (0.9)**	**708.38 (23.61)**	**0.8 (0.0)**	**49.19 (1.64)**	**0.8 (0.0)**	**770.54 (25.68)**	**237.47 (7.92)**	**1399.04 (46.63)**
Taking too little	21 (11.7)	0.023 (0.001)	-347.36 (-16.54)	22.8 (1.1)	18.5 (0.9)	429.13 (20.43)	0.6 (0.0)	37.27 (1.77)	0.5 (0.0)	534.90 (25.47)	180.87 (8.61)	834.81 (39.75)
Difficulty using dosage form	4 (2.2)	0.011 (0.003)	0.00 (0.00)	6.6 (1.6)	5.6 (1.4)	211.15 (52.79)	0.1 (0.0)	3.02 (0.76)	0.1 (0.0)	117.73 (29.43)	17.72 (4.43)	349.61 (87.40)

DRP type Subtype	Number (%) of DRPs	QOL lost (QALY)	Annual drug costs ($)	Days of ill health	Number of GP visits	Cost of GP visits ($)	Number of specialist visits	Cost of specialist visits ($)	Days in hospital	Cost of hospitalisation ($)	Cost of pathology investigations ($)	Total costs ($)
Other compliance problem	5 (2.8)	0.003 (0.001)	-19.19 (-3.84)	3.7 (0.7)	2.8 (0.6)	68.11 (13.62)	0.1 (0.0)	8.90 (1.78)	0.1 (0.0)	117.92 (23.58)	38.88 (7.78)	214.62 (42.92)
Untreated indications	**44 (24.4)**	**0.322 (0.007)**	**652.21 (14.82)**	**197.9 (4.5)**	**138.8 (3.2)**	**3767.82 (85.63)**	**8.4 (0.2)**	**502.91 (11.43)**	**8.0 (0.2)**	**7784.46 (176.92)**	**1979.90 (45.00)**	**14687.29 (333.80)**
Condition not adequately treated	28 (15.6)	0.229 (0.008)	167.74 (5.99)	128.8 (4.6)	95.2 (3.4)	2702.40 (96.51)	5.2 (0.2)	307.97 (11.00)	4.7 (0.2)	4508.83 (161.03)	1188.98 (42.46)	8875.92 (317.00)
Therapy required	16 (8.9)	0.093 (0.006)	484.47 (30.28)	69.1 (4.3)	43.6 (2.7)	1065.41 (66.59)	3.2 (0.2)	194.94 (12.18)	3.2 (0.2)	3275.62 (204.73)	790.92 (49.43)	5811.37 (363.21)
Monitoring	**16 (8.9)**	**0.016 (0.001)**	**0.00 (0.00)**	**11.9 (0.7)**	**14.1 (0.9)**	**349.87 (21.87)**	**0.5 (0.0)**	**32.76 (2.05)**	**0.2 (0.0)**	**220.68 (13.79)**	**155.70 (9.73)**	**759.00 (47.44)**
Laboratory monitoring	15 (8.3)	0.015 (0.001)	0.00 (0.00)	11.3 (0.8)	13.6 (0.9)	334.84 (22.32)	0.5 (0.0)	32.72 (2.18)	0.2 (0.0)	216.90 (14.46)	142.10 (9.47)	726.56 (48.44)
Non-laboratory monitoring	1 (0.6)	0.000 (0.000)	0.00 (0.00)	0.5 (0.5)	0.5 (0.5)	15.03 (15.03)	0.0 (0.0)	0.04 (0.04)	0.0 (0.0)	3.78 (3.78)	13.59 (13.59)	32.44 (32.44)
Education or information	**4 (2.2)**	**0.038 (0.010)**	**0.00 (0.00)**	**19.4 (4.8)**	**8.5 (2.1)**	**309.55 (77.39)**	**0.8 (0.2)**	**46.24 (11.56)**	**0.8 (0.2)**	**756.81 (189.20)**	**119.43 (29.86)**	**1232.02 (308.01)**
Patient drug information request	1 (0.6)	0.003 (0.003)	0.00 (0.00)	1.1 (1.1)	1.7 (1.7)	65.90 (65.90)	0.0 (0.0)	1.23 (1.23)	0.1 (0.1)	109.94 (109.94)	18.71 (18.71)	195.78 (195.78)
Confusion about therapy	1 (0.6)	0.001 (0.001)	0.00 (0.00)	1.3 (1.3)	1.0 (1.0)	23.26 (23.26)	0.0 (0.0)	1.29 (1.29)	0.0 (0.0)	19.28 (19.28)	5.46 (5.46)	49.30 (49.30)
Demonstration of device	2 (1.1)	0.035 (0.017)	0.00 (0.00)	17.0 (8.5)	5.8 (2.9)	220.38 (110.19)	0.7 (0.4)	43.71 (21.86)	0.7 (0.3)	627.60 (313.80)	95.25 (47.63)	986.95 (493.47)
Non-clinical	**1 (0.6)**	**0.001 (0.001)**	**0.00 (0.00)**	**0.7 (0.7)**	**1.7 (1.7)**	**64.70 (64.70)**	**0.0 (0.0)**	**1.92 (1.92)**	**0.0 (0.0)**	**46.35 (46.35)**	**12.40 (12.40)**	**125.38 (125.38)**
Dietary problem	1 (0.6)	0.001 (0.001)	0.00 (0.00)	0.7 (0.7)	1.7 (1.7)	64.70 (64.70)	0.0 (0.0)	1.92 (1.92)	0.0 (0.0)	46.35 (46.35)	12.40 (12.40)	125.38 (125.38)
Toxicity or adverse reaction	**22 (12.2)**	**0.053 (0.002)**	**213.13 (9.69)**	**29.9 (1.4)**	**32.2 (1.5)**	**1162.87 (52.86)**	**1.4 (0.1)**	**86.12 (3.91)**	**1.6 (0.1)**	**1584.73 (72.03)**	**418.29 (19.01)**	**3465.14**

DRP type Subtype	Number (%) of DRPs	QOL lost (QALY)	Annual drug costs ($)	Days of ill health	Number of GP visits	Cost of GP visits ($)	Number of specialist visits	Cost of specialist visits ($)	Days in hospital	Cost of hospitalisation ($)	Cost of pathology investigations ($)	Total costs ($)
												(157.51)
Toxicity caused by dose	3 (1.7)	0.003 (0.001)	-260.87 (-86.96)	3.1 (1.0)	4.6 (1.5)	179.91 (59.97)	0.1 (0.0)	6.05 (2.02)	0.1 (0.0)	128.55 (42.85)	60.86 (20.29)	114.49 (38.16)
Toxicity caused by drug interaction	3 (1.7)	0.002 (0.001)	338.75 (112.92)	2.0 (0.7)	2.5 (0.8)	96.61 (32.20)	0.1 (0.0)	3.29 (1.10)	0.1 (0.0)	86.30 (28.77)	27.12 (9.04)	552.07 (184.02)
Toxicity evident	14 (7.8)	0.047 (0.003)	-323.62 (-23.12)	24.6 (1.8)	24.7 (1.8)	873.53 (62.39)	1.3 (0.1)	76.10 (5.44)	1.4 (0.1)	1356.25 (96.88)	322.91 (23.06)	2305.16 (164.65)
Other toxicity/adverse effect problem	2 (1.1)	0.000 (0.000)	458.88 (229.44)	0.1 (0.1)	0.3 (0.2)	12.82 (6.41)	0.0 (0.0)	0.68 (0.34)	0.0 (0.0)	13.63 (6.82)	7.40 (3.70)	493.42 (246.71)
Total	**180 (100.0)**	**0.673 (0.004)**	**-1565.51 (-8.70)**	**429.6 (2.4)**	**324.0 (1.8)**	**9352.25 (51.96)**	**18.9 (0.1)**	**1138.37 (6.32)**	**17.4 (0.1)**	**16978.46 (94.32)**	**4254.44 (23.64)**	**30158.00 (167.54)**

TABLE 168 - BASELINE SCENARIO - ESTIMATED QOL AND RESOURCE UTILISATION WITHOUT HMR IN DATASET OF 120 PANEL-SPECIFIC HMRS

PANEL	HMR	QOL LOST (QALY)	ANNUAL DRUG COSTS ($)	DAYS OF ILL HEALTH	NUMBER (COST, $) OF GP VISITS	NUMBER (COST, $) OF SPECIALIST VISITS	DAYS IN HOSPITAL	COST OF HOSPITALISATION ($)	COST OF PATHOLOGY INVESTIGATIONS ($)	TOTAL COSTS ($)
1	4	0.091	1478.47	36.6	12.5 (248.65)	1.4 (78.82)	1.3	1421.74	177.72	3405.40
1	24	0.037	1210.89	15.4	9.2 (349.55)	1.0 (58.25)	1.2	1176.83	285.03	3080.54
1	45	0.022	1773.43	8.9	4.1 (139.03)	0.3 (14.81)	0.4	388.05	109.61	2424.94
1	58	0.056	8705.28	23.1	13.4 (471.97)	1.2 (66.86)	1.1	1443.93	161.64	10849.68
1	75	0.025	2336.70	9.8	3.7 (121.65)	0.6 (35.52)	0.7	771.64	154.85	3420.36
1	78	0.004	1770.27	1.8	1.4 (54.43)	0.1 (4.02)	0.1	134.26	27.15	1990.13
1	114	0.007	2109.70	2.9	3.2 (116.29)	0.1 (4.83)	0.1	97.48	38.54	2366.84
1	143	0.007	2018.00	3.3	2.0 (72.56)	0.2 (8.14)	0.2	229.06	48.31	2376.07
1	145	0.005	3615.66	12.6	12.1 (156.89)	0.2 (9.29)	0.1	87.47	60.97	3930.28
1	165	0.002	1236.80	1.9	1.6 (63.97)	0.3 (18.87)	0.1	56.78	22.76	1399.18
1	186	0.002	1630.24	1.6	5.3 (209.23)	0.3 (17.65)	0.2	128.64	23.78	2009.55
1	223	0.026	1879.71	15.8	11.8 (160.20)	0.6 (36.50)	0.3	241.49	101.36	2419.26
1	226	0.002	960.26	2.5	0.8 (27.99)	0.0 (0.19)	0.2	175.05	27.44	1190.93
1	250	0.003	1912.64	1.5	2.1 (75.99)	0.2 (9.28)	0.1	127.14	52.31	2177.35
1	255	0.006	3259.66	2.6	2.4 (73.52)	0.3 (15.84)	0.1	196.93	37.64	3583.60
1	270	0.003	1070.17	1.8	1.8 (72.70)	0.2 (11.91)	0.2	190.61	19.46	1364.85
1	278	0.007	2674.19	3.6	5.7 (226.63)	0.2 (12.22)	0.3	296.56	59.80	3269.41
1	340	0.005	2711.09	2.3	1.4 (57.31)	0.1 (7.29)	0.3	275.07	54.55	3105.32
1	367	0.039	2552.32	14.1	7.9 (275.03)	0.6 (33.65)	0.8	823.13	110.61	3794.73

PANEL	HMR	QOL LOST (QALY)	ANNUAL DRUG COSTS ($)	DAYS OF ILL HEALTH	NUMBER (COST, $) OF GP VISITS	NUMBER (COST, $) OF SPECIALIST VISITS	DAYS IN HOSPITAL	COST OF HOSPITALISATION ($)	COST OF PATHOLOGY INVESTIGATIONS ($)	TOTAL COSTS ($)
1	385	0.008	3668.80	4.5	6.5 (221.03)	0.5 (34.79)	0.4	409.89	99.93	4434.44
1	414	0.002	1529.25	1.1	0.8 (32.69)	0.0 (1.54)	0.0	31.13	3.45	1598.07
1	545	0.014	682.99	7.5	5.2 (73.36)	0.1 (5.55)	0.1	72.97	44.94	879.81
1	555	0.005	1649.16	2.8	0.9 (30.14)	0.0 (0.12)	0.1	90.59	10.89	1780.89
1	584	0.000	840.46	0.0	0.0 (0.00)	0.0 (0.00)	0.0	0.00	0.00	840.46
1	587	0.018	2220.27	11.3	6.6 (183.71)	0.3 (17.21)	0.5	483.59	74.67	2979.45
1	597	0.009	1323.22	4.5	7.6 (295.44)	0.3 (15.77)	0.4	355.52	99.41	2089.35
1	665	0.001	2192.44	1.7	0.9 (34.62)	0.0 (3.01)	0.0	17.46	7.11	2254.64
1	669	0.009	12658.22	11.7	8.3 (136.36)	0.4 (26.55)	0.3	303.30	88.07	13212.50
1	681	0.018	3550.54	8.1	6.9 (197.39)	0.9 (55.37)	0.6	656.54	159.05	4618.90
1	684	0.027	1209.12	9.2	4.4 (159.40)	0.3 (14.22)	0.3	498.55	10.70	1891.99
2	5	0.005	1441.66	2.8	1.1 (44.58)	0.4 (23.28)	0.3	274.12	27.36	1811.00
2	53	0.235	2966.70	92.5	35.3 (1144.34)	3.2 (181.69)	4.8	5174.51	640.22	10107.45
2	126	0.023	3299.35	30.9	16.7 (334.74)	0.8 (48.20)	0.8	678.40	210.23	4570.92
2	153	0.013	1637.67	7.8	10.7 (293.80)	0.3 (14.77)	0.1	57.82	57.98	2062.05
2	187	0.042	2153.64	16.4	10.1 (348.80)	1.0 (60.36)	1.0	1287.67	201.94	4052.41
2	236	0.003	1642.68	5.1	3.2 (60.89)	0.1 (7.81)	0.2	194.83	61.70	1967.91
2	238	0.006	3207.96	3.1	4.0 (153.23)	0.2 (14.11)	0.4	417.65	61.10	3854.04
2	249	0.005	1631.70	44.4	30.5 (391.88)	0.7 (44.79)	0.2	229.40	224.46	2522.23
2	251	0.006	4102.33	3.1	5.0 (196.90)	0.3 (19.25)	0.5	436.52	77.26	4832.26

PANEL	HMR	QOL LOST (QALY)	ANNUAL DRUG COSTS ($)	DAYS OF ILL HEALTH	NUMBER (COST, $) OF GP VISITS	NUMBER (COST, $) OF SPECIALIST VISITS	DAYS IN HOSPITAL	COST OF HOSPITALISATION ($)	COST OF PATHOLOGY INVESTIGATIONS ($)	TOTAL COSTS ($)
2	343	0.003	1693.21	14.8	12.0 (133.86)	0.2 (11.74)	0.1	104.42	73.88	2017.10
2	369	0.004	2474.22	2.0	3.4 (125.65)	0.0 (1.97)	0.0	49.73	1.69	2653.26
2	378	0.060	3761.81	35.0	25.1 (407.63)	1.3 (79.78)	0.5	397.46	214.14	4860.83
2	383	0.016	2412.18	10.8	15.9 (586.63)	0.6 (36.92)	0.7	629.81	162.41	3827.95
2	384	0.005	2194.15	4.3	7.0 (262.73)	0.3 (19.65)	0.1	110.85	106.00	2693.38
2	409	0.009	2831.20	7.4	9.7 (299.28)	0.5 (35.87)	0.3	316.42	156.12	3638.88
2	411	0.004	2375.92	2.5	5.5 (179.39)	0.2 (10.03)	0.0	18.76	71.67	2655.77
2	415	0.026	3896.70	19.1	15.0 (232.10)	0.7 (45.92)	0.3	246.32	150.39	4571.43
2	431	0.004	1387.56	2.1	2.2 (65.09)	0.3 (17.28)	0.2	178.58	38.84	1687.36
2	433	0.012	3112.80	5.0	4.8 (179.45)	0.2 (10.54)	0.3	355.69	31.30	3689.78
2	448	0.001	1938.46	0.8	1.4 (55.10)	0.3 (21.46)	0.0	35.64	47.61	2098.27
2	477	0.011	2345.81	6.5	6.9 (250.14)	0.1 (4.91)	0.1	225.60	28.52	2854.98
2	504	0.009	2103.72	6.4	7.6 (143.37)	0.2 (14.05)	0.1	59.60	54.48	2375.21
2	511	0.042	17008.95	27.3	22.4 (361.58)	1.0 (67.19)	0.3	294.09	181.70	17913.52
2	514	0.036	1026.61	20.5	20.1 (523.86)	1.4 (90.91)	0.8	744.58	351.83	2737.78
2	519	0.033	1531.26	18.1	14.4 (241.48)	0.5 (30.92)	0.4	332.52	168.65	2304.84
2	563	0.015	1152.18	7.2	6.8 (247.32)	0.3 (19.22)	0.1	196.34	109.43	1724.49
2	570	0.011	2743.26	8.4	10.7 (224.55)	0.5 (33.19)	0.1	109.57	94.19	3204.77
2	585	0.021	2502.80	8.4	9.0 (324.11)	0.5 (30.42)	0.7	717.69	171.96	3746.98
2	616	0.008	3402.03	3.5	5.4 (208.16)	0.3 (15.61)	0.3	241.00	115.62	3982.41

PANEL	HMR	QOL LOST (QALY)	ANNUAL DRUG COSTS ($)	DAYS OF ILL HEALTH	NUMBER (COST, $) OF GP VISITS	NUMBER (COST, $) OF SPECIALIST VISITS	DAYS IN HOSPITAL	COST OF HOSPITALISATION ($)	COST OF PATHOLOGY INVESTIGATIONS ($)	TOTAL COSTS ($)
2	639	0.009	3534.03	6.0	10.4 (355.87)	0.2 (9.64)	0.1	140.35	76.38	4116.27
3	6	0.000	3237.18	0.0	0.0 (0.00)	0.0 (0.00)	0.0	0.00	0.00	3237.18
3	14	0.000	790.21	0.0	0.0 (0.00)	0.0 (0.00)	0.0	0.00	0.00	790.21
3	16	0.000	893.43	0.3	0.4 (14.13)	0.0 (2.39)	0.0	37.63	6.17	953.75
3	18	0.000	2208.38	0.2	0.2 (8.41)	0.0 (0.61)	0.0	16.72	4.82	2238.94
3	50	0.000	3278.64	0.0	0.0 (0.00)	0.0 (0.00)	0.0	0.00	0.00	3278.64
3	82	0.002	1993.67	1.2	0.7 (24.02)	0.1 (7.29)	0.1	101.31	10.70	2136.99
3	89	0.001	1410.53	0.6	0.9 (35.34)	0.0 (0.02)	0.0	17.41	9.23	1472.52
3	104	0.000	1576.74	0.0	0.0 (0.00)	0.0 (0.00)	0.0	0.00	0.00	1576.74
3	110	0.000	2135.79	0.3	0.5 (17.01)	0.0 (1.32)	0.0	27.90	7.73	2189.76
3	124	0.000	3486.11	0.0	0.0 (0.00)	0.0 (0.00)	0.0	0.00	0.00	3486.11
3	140	0.017	2445.12	6.4	2.3 (93.94)	0.4 (21.19)	0.7	628.14	150.90	3339.28
3	144	0.000	1616.28	0.0	0.0 (0.00)	0.0 (0.00)	0.0	0.00	0.00	1616.28
3	156	0.000	1313.11	0.1	0.1 (4.25)	0.0 (0.50)	0.0	14.52	0.90	1333.28
3	230	0.000	1322.88	0.2	0.1 (5.22)	0.0 (0.01)	0.0	18.76	2.00	1348.87
3	291	0.000	859.23	0.0	0.0 (0.00)	0.0 (0.00)	0.0	0.00	0.00	859.23
3	310	0.001	4516.90	0.4	0.1 (4.10)	0.0 (0.63)	0.0	25.17	4.76	4551.56
3	331	0.000	1082.39	0.0	0.0 (0.75)	0.0 (0.24)	0.0	0.00	0.18	1083.57
3	360	0.004	548.03	8.5	0.7 (27.06)	0.2 (16.68)	0.0	52.06	15.14	658.98
3	393	0.004	1008.72	5.6	0.0 (0.00)	0.0 (0.30)	0.0	3.51	26.76	1039.30

PANEL	HMR	QOL LOST (QALY)	ANNUAL DRUG COSTS ($)	DAYS OF ILL HEALTH	NUMBER (COST, $) OF GP VISITS	NUMBER (COST, $) OF SPECIALIST VISITS	DAYS IN HOSPITAL	COST OF HOSPITALISATION ($)	COST OF PATHOLOGY INVESTIGATIONS ($)	TOTAL COSTS ($)
3	402	0.029	2977.01	22.3	4.8 (190.79)	2.3 (134.03)	2.1	1992.17	169.45	5463.44
3	441	0.007	2311.08	4.4	0.0 (0.00)	0.0 (0.00)	0.0	0.00	0.00	2311.08
3	473	0.001	1856.86	2.7	2.2 (58.18)	0.1 (5.58)	0.1	56.06	78.04	2054.72
3	496	0.001	1879.68	0.7	0.6 (16.36)	0.2 (12.28)	0.0	18.99	31.50	1958.81
3	559	0.000	4117.29	0.3	0.0 (0.00)	0.0 (2.37)	0.0	0.00	2.16	4121.82
3	564	0.000	449.72	1.5	0.2 (10.07)	0.2 (14.60)	0.0	0.00	24.61	498.99
3	576	0.000	2771.59	0.0	0.0 (0.00)	0.0 (0.00)	0.0	0.00	0.00	2771.59
3	596	0.002	1597.46	2.0	0.3 (12.92)	0.1 (4.04)	0.1	58.52	14.54	1687.47
3	602	0.007	817.31	5.5	0.7 (26.54)	0.0 (2.34)	0.0	25.22	37.84	909.26
3	636	0.005	2894.45	3.1	2.1 (85.59)	0.3 (17.60)	0.2	184.58	22.58	3204.80
3	683	0.057	578.66	30.8	8.1 (333.36)	3.3 (174.08)	3.5	2995.97	238.49	4320.56
4	15	0.002	1825.10	0.7	0.7 (18.70)	0.0 (1.33)	0.0	22.56	2.05	1869.74
4	23	0.007	1223.16	5.8	5.2 (196.32)	0.5 (32.89)	0.2	163.72	46.32	1662.41
4	39	0.003	3248.51	1.5	0.9 (20.20)	0.1 (3.70)	0.1	55.55	10.51	3338.47
4	40	0.003	362.61	1.7	2.3 (84.67)	0.1 (7.83)	0.1	75.35	15.43	545.89
4	66	0.006	5339.67	2.8	1.1 (40.19)	0.1 (7.23)	0.0	13.73	14.64	5415.46
4	72	0.017	2687.53	7.9	7.5 (232.24)	0.4 (21.33)	0.4	521.51	111.63	3574.23
4	92	0.000	1420.39	0.2	1.4 (54.60)	0.0 (0.86)	0.0	25.65	16.87	1518.37
4	138	0.041	1973.88	23.1	6.5 (227.51)	0.6 (31.88)	1.4	1194.39	113.27	3540.93
4	170	0.003	610.76	1.5	0.4 (15.32)	0.1 (6.14)	0.2	157.82	18.96	809.00

PANEL	HMR	QOL LOST (QALY)	ANNUAL DRUG COSTS ($)	DAYS OF ILL HEALTH	NUMBER (COST, $) OF GP VISITS	NUMBER (COST, $) OF SPECIALIST VISITS	DAYS IN HOSPITAL	COST OF HOSPITALISATION ($)	COST OF PATHOLOGY INVESTIGATIONS ($)	TOTAL COSTS ($)
4	172	0.001	2401.45	0.8	1.6 (56.27)	0.0 (0.69)	0.0	13.51	9.09	2481.01
4	209	0.009	1876.47	4.9	3.6 (141.04)	0.4 (18.92)	0.4	306.73	103.56	2446.71
4	222	0.010	1153.36	5.3	3.0 (112.57)	0.4 (23.70)	0.1	47.27	14.29	1351.19
4	261	0.000	2642.86	0.8	1.7 (54.46)	0.0 (1.57)	0.0	21.96	29.31	2750.16
4	281	0.019	4160.46	7.1	1.6 (37.64)	0.2 (12.53)	0.4	295.46	39.33	4545.42
4	297	0.010	1356.34	5.6	9.8 (330.15)	0.7 (45.44)	0.4	442.08	103.04	2277.04
4	299	0.000	990.40	0.0	0.0 (0.00)	0.0 (0.00)	0.0	0.00	0.00	990.40
4	345	0.001	1882.85	0.5	2.9 (108.40)	0.0 (0.72)	0.0	24.50	11.85	2028.31
4	348	0.011	1254.86	4.2	3.2 (89.60)	0.3 (22.20)	0.2	297.35	43.73	1707.74
4	404	0.015	2372.35	11.2	12.5 (340.53)	0.6 (43.05)	0.3	243.61	124.69	3124.23
4	426	0.003	3276.38	2.1	3.4 (109.15)	0.2 (10.33)	0.0	27.87	21.35	3445.08
4	436	0.014	2302.55	11.5	5.0 (122.09)	0.1 (5.77)	0.2	221.65	46.79	2698.86
4	440	0.008	3270.36	5.0	8.0 (223.43)	0.2 (12.34)	0.1	79.31	47.65	3633.09
4	447	0.007	3948.05	13.0	14.7 (282.62)	0.1 (5.56)	0.0	32.88	51.89	4321.00
4	488	0.003	3565.83	2.8	6.1 (234.41)	0.1 (3.85)	0.0	30.17	55.78	3890.04
4	499	0.006	1583.85	5.4	8.1 (323.80)	0.5 (35.41)	0.2	229.75	93.21	2266.02
4	524	0.002	2785.31	2.1	2.7 (102.97)	0.0 (2.93)	0.1	57.46	20.43	2969.10
4	603	0.000	3189.48	0.1	0.9 (34.46)	0.0 (0.50)	0.0	14.82	5.80	3245.06
4	613	0.001	1428.24	0.3	0.2 (9.14)	0.0 (0.52)	0.0	14.16	7.17	1459.23
4	618	0.001	708.44	0.8	1.9 (67.39)	0.1 (3.39)	0.0	17.97	18.27	815.46

PANEL	HMR	QOL LOST (QALY)	ANNUAL DRUG COSTS ($)	DAYS OF ILL HEALTH	NUMBER (COST, $) OF GP VISITS	NUMBER (COST, $) OF SPECIALIST VISITS	DAYS IN HOSPITAL	COST OF HOSPITALISATION ($)	COST OF PATHOLOGY INVESTIGATIONS ($)	TOTAL COSTS ($)
4	676	0.002	2185.79	1.3	3.4 (120.39)	0.1 (8.32)	0.1	87.07	47.94	2449.51
	Total	**1.485**	**288944.22**	**874.1**	**627.7 (17472.57)**	**40.1 (2428.54)**	**36.2**	**36447.84**	**8244.16**	**353537.32**

TABLE 169 - BASELINE SCENARIO - ESTIMATED QOL AND RESOURCE UTILISATION WITH HMR IN DATASET OF 120 PANEL-SPECIFIC HMRS

PANEL	HMR	QOL LOST (QALY)	ANNUAL DRUG COSTS ($)	DAYS OF ILL HEALTH	NUMBER (COST, $) OF GP VISITS	NUMBER (COST, $) OF SPECIALIST VISITS	DAYS IN HOSPITAL	COST OF HOSPITALISATION ($)	COST OF PATHOLOGY INVESTIGATIONS ($)	HMR cost ($)	TOTAL COSTS ($)
1	4	0.095	1524.35	38.5	13.8 (273.14)	1.5 (85.21)	1.4	1491.17	200.31	323.80	3897.99
1	24	0.032	970.81	13.7	8.7 (331.64)	0.9 (53.67)	1.1	1059.87	259.47	323.80	2999.27
1	45	0.022	1773.43	8.6	3.9 (133.28)	0.3 (16.54)	0.4	430.60	111.69	323.80	2789.34
1	58	0.056	8640.77	22.8	12.9 (456.88)	1.2 (65.64)	1.1	1433.90	151.17	323.80	11072.17
1	75	0.020	2336.70	8.0	3.2 (105.08)	0.5 (28.50)	0.6	596.43	123.20	323.80	3513.71
1	78	0.004	1773.86	1.8	1.4 (56.48)	0.1 (3.77)	0.1	130.66	26.74	323.80	2315.30
1	114	0.007	2123.70	2.8	3.0 (105.78)	0.1 (3.86)	0.1	92.36	37.58	323.80	2687.07
1	143	0.007	2054.35	3.1	2.1 (76.90)	0.1 (7.23)	0.2	225.00	46.01	323.80	2733.29
1	145	0.004	3605.65	11.9	12.1 (150.75)	0.1 (7.34)	0.1	64.17	59.34	323.80	4211.04
1	165	0.002	1236.80	1.3	1.7 (67.10)	0.2 (13.18)	0.1	53.65	16.96	323.80	1711.50
1	186	0.002	1630.24	1.1	3.7 (146.28)	0.2 (12.33)	0.1	92.54	15.83	323.80	2221.02
1	223	0.021	1944.96	12.6	9.2 (124.14)	0.4 (28.70)	0.2	189.68	76.42	323.80	2687.71
1	226	0.002	968.75	2.3	0.8 (25.62)	0.0 (0.17)	0.2	161.34	24.91	323.80	1504.59
1	250	0.003	1912.64	1.5	2.1 (74.18)	0.2 (9.45)	0.1	130.38	51.96	323.80	2502.41
1	255	0.005	3097.18	2.3	2.0 (62.12)	0.2 (14.13)	0.1	176.01	34.26	323.80	3707.50
1	270	0.003	1086.42	1.5	1.7 (65.42)	0.2 (9.89)	0.2	168.40	16.73	323.80	1670.67
1	278	0.007	2479.16	3.4	5.5 (216.73)	0.2 (10.73)	0.3	268.64	54.39	323.80	3353.45
1	340	0.005	2711.09	2.3	1.4 (55.02)	0.1 (7.41)	0.3	277.14	54.90	323.80	3429.36
1	367	0.035	2570.64	12.7	7.3 (256.77)	0.6 (31.66)	0.7	753.15	105.08	323.80	4041.10

PANEL	HMR	QOL LOST (QALY)	ANNUAL DRUG COSTS ($)	DAYS OF ILL HEALTH	NUMBER (COST, $) OF GP VISITS	NUMBER (COST, $) OF SPECIALIST VISITS	DAYS IN HOSPITAL	COST OF HOSPITALISATION ($)	COST OF PATHOLOGY INVESTIGATIONS ($)	HMR cost ($)	TOTAL COSTS ($)
1	385	0.008	3731.62	4.3	6.5 (219.18)	0.5 (33.86)	0.4	395.22	95.71	323.80	4799.40
1	414	0.002	1529.25	1.0	0.8 (31.87)	0.0 (1.51)	0.0	30.35	3.37	323.80	1920.14
1	545	0.013	748.76	6.9	4.8 (68.91)	0.1 (5.17)	0.1	65.17	41.29	323.80	1253.10
1	555	0.005	1649.16	2.5	0.9 (28.50)	0.0 (0.11)	0.1	81.17	10.02	323.80	2092.76
1	584	0.000	766.87	0.0	0.0 (0.00)	0.0 (0.00)	0.0	0.00	0.00	323.80	1090.67
1	587	0.017	2169.37	10.1	6.0 (174.16)	0.3 (15.55)	0.5	448.37	64.35	323.80	3195.61
1	597	0.009	1323.22	4.4	7.5 (288.87)	0.3 (15.13)	0.3	338.90	90.30	323.80	2380.21
1	665	0.001	1964.98	1.3	0.6 (24.16)	0.0 (2.19)	0.0	10.65	4.67	323.80	2330.44
1	669	0.008	12415.24	10.3	7.1 (115.28)	0.4 (22.29)	0.2	255.03	74.01	323.80	13205.65
1	681	0.017	3614.49	7.8	6.7 (188.89)	0.9 (54.46)	0.5	633.00	154.49	323.80	4969.13
1	684	0.025	1209.12	8.8	4.3 (155.40)	0.3 (13.69)	0.3	475.64	10.23	323.80	2187.88
2	5	0.003	1673.06	1.2	0.5 (19.38)	0.2 (9.62)	0.1	128.68	14.38	323.80	2168.92
2	53	0.200	3100.10	82.1	31.1 (1059.59)	3.1 (172.87)	4.8	5160.30	645.79	323.80	10462.45
2	126	0.026	3267.37	30.4	16.3 (321.25)	0.8 (45.96)	0.8	697.86	207.35	323.80	4863.59
2	153	0.011	1637.67	7.0	9.7 (273.45)	0.2 (12.82)	0.1	54.16	54.59	323.80	2356.49
2	187	0.037	2155.97	14.2	8.8 (303.66)	0.9 (54.68)	1.0	1167.69	191.03	323.80	4196.83
2	236	0.002	1642.68	4.5	2.8 (46.19)	0.1 (6.35)	0.2	142.66	45.46	323.80	2207.13
2	238	0.005	3207.96	2.7	3.6 (140.10)	0.2 (12.20)	0.4	360.92	53.51	323.80	4098.49
2	249	0.005	1528.56	42.8	29.4 (373.31)	0.6 (42.88)	0.2	215.80	212.61	323.80	2696.96
2	251	0.005	4102.33	2.4	4.5 (178.99)	0.2 (15.26)	0.4	328.47	60.36	323.80	5009.21

PANEL	HMR	QOL LOST (QALY)	ANNUAL DRUG COSTS ($)	DAYS OF ILL HEALTH	NUMBER (COST, $) OF GP VISITS	NUMBER (COST, $) OF SPECIALIST VISITS	DAYS IN HOSPITAL	COST OF HOSPITALISATION ($)	COST OF PATHOLOGY INVESTIGATIONS ($)	HMR cost ($)	TOTAL COSTS ($)
2	343	0.003	1693.21	12.7	10.9 (123.09)	0.2 (9.56)	0.1	96.99	66.29	323.80	2312.95
2	369	0.003	2474.22	1.6	2.7 (100.90)	0.0 (1.48)	0.0	35.97	1.50	323.80	2937.87
2	378	0.060	3769.72	34.6	24.4 (400.36)	1.2 (78.97)	0.5	400.72	210.81	323.80	5184.38
2	383	0.011	2412.18	8.4	14.9 (552.57)	0.6 (33.99)	0.5	455.47	132.81	323.80	3910.82
2	384	0.004	2224.64	3.3	6.5 (242.15)	0.2 (14.64)	0.1	88.48	82.52	323.80	2976.21
2	409	0.009	2781.51	7.7	9.0 (273.86)	0.5 (32.67)	0.3	333.53	158.19	323.80	3903.57
2	411	0.001	2375.92	1.2	4.2 (147.80)	0.1 (5.08)	0.0	3.01	60.02	323.80	2915.63
2	415	0.017	3896.70	13.8	12.6 (192.92)	0.5 (32.45)	0.2	169.11	105.28	323.80	4720.26
2	431	0.004	1387.56	2.1	2.2 (62.82)	0.3 (17.94)	0.2	176.66	41.06	323.80	2009.83
2	433	0.012	3112.80	4.8	3.9 (147.54)	0.2 (9.45)	0.2	323.95	24.21	323.80	3941.75
2	448	0.001	1857.59	0.6	1.1 (39.59)	0.3 (21.23)	0.0	32.27	39.35	323.80	2313.84
2	477	0.006	2483.96	4.3	6.0 (219.17)	0.1 (3.43)	0.1	148.72	28.58	323.80	3207.65
2	504	0.007	2103.72	5.1	6.3 (117.09)	0.2 (11.13)	0.0	42.03	43.65	323.80	2641.42
2	511	0.046	17044.77	29.0	22.4 (354.23)	1.1 (69.89)	0.4	317.40	185.17	323.80	18295.26
2	514	0.025	1026.61	14.0	15.5 (417.14)	1.0 (66.79)	0.5	501.65	267.89	323.80	2603.87
2	519	0.034	1001.88	18.9	15.3 (257.87)	0.5 (33.40)	0.4	357.32	181.00	323.80	2155.27
2	563	0.013	1152.18	6.6	6.5 (238.58)	0.3 (16.63)	0.1	172.83	95.04	323.80	1999.05
2	570	0.010	2743.26	7.5	9.3 (187.54)	0.4 (30.41)	0.1	94.72	81.85	323.80	3461.58
2	585	0.019	2493.89	7.7	9.2 (329.14)	0.5 (27.42)	0.7	645.05	157.89	323.80	3977.19
2	616	0.007	3355.34	3.3	5.1 (195.26)	0.2 (14.19)	0.2	218.66	103.27	323.80	4210.52

PANEL	HMR	QOL LOST (QALY)	ANNUAL DRUG COSTS ($)	DAYS OF ILL HEALTH	NUMBER (COST, $) OF GP VISITS	NUMBER (COST, $) OF SPECIALIST VISITS	DAYS IN HOSPITAL	COST OF HOSPITALISATION ($)	COST OF PATHOLOGY INVESTIGATIONS ($)	HMR cost ($)	TOTAL COSTS ($)
2	639	0.010	3494.54	6.1	8.8 (281.38)	0.2 (11.12)	0.1	121.45	66.83	323.80	4299.12
3	6	0.000	3374.06	0.0	0.0 (0.00)	0.0 (0.00)	0.0	0.00	0.00	323.80	3697.86
3	14	0.000	747.54	0.0	0.0 (0.00)	0.0 (0.00)	0.0	0.00	0.00	323.80	1071.34
3	16	0.001	903.06	0.4	0.5 (20.69)	0.1 (3.17)	0.0	51.32	8.19	323.80	1310.22
3	18	0.000	2316.95	0.4	0.3 (11.65)	0.0 (1.09)	0.0	33.28	7.88	323.80	2694.64
3	50	0.000	2798.30	0.0	0.0 (0.00)	0.0 (0.00)	0.0	0.00	0.00	323.80	3122.10
3	82	0.003	2002.19	1.5	0.8 (28.85)	0.2 (9.11)	0.1	130.10	13.05	323.80	2507.10
3	89	0.001	1285.66	0.9	1.3 (53.68)	0.0 (0.03)	0.0	31.98	14.35	323.80	1709.50
3	104	0.000	1673.62	0.0	0.0 (0.00)	0.0 (0.00)	0.0	0.00	0.00	323.80	1997.42
3	110	0.000	2135.79	0.6	1.3 (44.85)	0.1 (2.69)	0.1	56.56	18.20	323.80	2581.88
3	124	0.000	3448.33	0.0	0.0 (0.00)	0.0 (0.00)	0.0	0.00	0.00	323.80	3772.13
3	140	0.031	2445.12	11.4	3.3 (134.20)	0.5 (30.37)	1.2	1055.54	231.08	323.80	4220.10
3	144	0.000	1616.28	0.0	0.0 (0.00)	0.0 (0.00)	0.0	0.00	0.00	323.80	1940.08
3	156	0.000	844.60	0.2	0.2 (6.71)	0.0 (0.79)	0.0	22.92	1.35	323.80	1200.16
3	230	0.000	1322.88	0.2	0.2 (7.83)	0.0 (0.01)	0.0	28.13	2.81	323.80	1685.46
3	291	0.000	798.66	0.0	0.0 (0.00)	0.0 (0.00)	0.0	0.00	0.00	323.80	1122.46
3	310	0.002	4707.70	0.8	0.2 (6.15)	0.0 (1.08)	0.1	56.63	8.62	323.80	5103.98
3	331	0.000	1273.95	0.1	0.1 (5.03)	0.0 (1.58)	0.0	0.00	1.21	323.80	1605.57
3	360	0.009	180.06	11.7	1.7 (61.51)	0.3 (23.07)	0.1	125.18	18.44	323.80	732.06
3	393	0.002	1008.72	1.1	0.0 (0.00)	0.0 (0.05)	0.0	26.34	5.14	323.80	1364.05

PANEL	HMR	QOL LOST (QALY)	ANNUAL DRUG COSTS ($)	DAYS OF ILL HEALTH	NUMBER (COST, $) OF GP VISITS	NUMBER (COST, $) OF SPECIALIST VISITS	DAYS IN HOSPITAL	COST OF HOSPITALISATION ($)	COST OF PATHOLOGY INVESTIGATIONS ($)	HMR cost ($)	TOTAL COSTS ($)
3	402	0.022	2753.09	15.3	1.9 (74.93)	0.9 (55.01)	0.3	257.18	116.17	323.80	3580.18
3	441	0.003	2408.28	2.3	0.0 (0.00)	0.0 (0.00)	0.0	0.00	0.00	323.80	2732.08
3	473	0.002	1856.86	2.6	2.7 (88.35)	0.1 (8.07)	0.1	132.30	57.16	323.80	2466.54
3	496	0.000	1756.57	0.4	0.5 (14.54)	0.0 (1.33)	0.0	28.13	5.33	323.80	2129.70
3	559	0.000	4117.29	0.0	0.0 (0.00)	0.0 (0.00)	0.0	0.00	0.00	323.80	4441.09
3	564	0.000	449.72	0.8	0.0 (0.00)	0.1 (3.95)	0.0	0.00	6.87	323.80	784.34
3	576	0.000	2771.59	0.0	0.0 (0.00)	0.0 (0.00)	0.0	0.00	0.00	323.80	3095.39
3	596	0.003	1630.23	2.6	0.6 (24.60)	0.1 (5.06)	0.1	94.38	24.37	323.80	2102.44
3	602	0.004	658.16	3.1	0.7 (26.84)	0.1 (3.96)	0.0	42.63	25.91	323.80	1081.30
3	636	0.002	2894.45	1.2	1.1 (44.17)	0.1 (5.29)	0.1	72.14	10.94	323.80	3350.79
3	683	0.049	578.66	26.4	6.6 (275.33)	2.8 (148.56)	3.0	2588.58	199.84	323.80	4114.78
4	15	0.003	1911.43	1.0	0.7 (20.61)	0.0 (1.79)	0.0	48.14	1.49	323.80	2307.25
4	23	0.010	1182.55	6.0	4.2 (153.45)	0.3 (18.38)	0.1	106.92	32.98	323.80	1818.08
4	39	0.004	3282.24	2.0	1.1 (28.85)	0.1 (5.37)	0.1	127.02	16.88	323.80	3784.16
4	40	0.004	416.56	1.5	1.2 (41.83)	0.1 (6.90)	0.1	70.40	14.70	323.80	874.19
4	66	0.009	5339.67	3.7	1.5 (56.23)	0.2 (9.27)	0.0	18.56	18.86	323.80	5766.39
4	72	0.012	2665.39	5.6	5.9 (190.83)	0.2 (13.71)	0.3	364.45	79.53	323.80	3637.71
4	92	0.001	1420.39	0.3	1.6 (61.74)	0.0 (1.48)	0.0	44.23	20.81	323.80	1872.45
4	138	0.062	1973.88	36.0	7.1 (254.11)	1.1 (63.62)	2.4	2172.60	164.26	323.80	4952.26
4	170	0.003	610.76	1.2	0.3 (12.41)	0.1 (5.05)	0.1	128.58	15.00	323.80	1095.60

PANEL	HMR	QOL LOST (QALY)	ANNUAL DRUG COSTS ($)	DAYS OF ILL HEALTH	NUMBER (COST, $) OF GP VISITS	NUMBER (COST, $) OF SPECIALIST VISITS	DAYS IN HOSPITAL	COST OF HOSPITALISATION ($)	COST OF PATHOLOGY INVESTIGATIONS ($)	HMR cost ($)	TOTAL COSTS ($)
4	172	0.001	2401.45	0.7	1.2 (43.95)	0.0 (0.61)	0.0	11.98	6.86	323.80	2788.65
4	209	0.008	1906.55	4.5	2.3 (92.87)	0.3 (17.40)	0.3	281.22	76.47	323.80	2698.31
4	222	0.011	1293.06	5.0	2.2 (83.04)	0.3 (17.71)	0.0	38.86	16.03	323.80	1772.50
4	261	0.000	2642.86	0.4	1.1 (37.74)	0.0 (0.89)	0.0	12.14	18.92	323.80	3036.35
4	281	0.016	5895.25	5.9	1.4 (35.59)	0.2 (10.03)	0.4	269.12	36.34	323.80	6570.13
4	297	0.011	1263.24	6.5	10.0 (340.31)	0.7 (47.64)	0.5	520.62	104.48	323.80	2600.08
4	299	0.000	990.40	0.0	0.0 (0.00)	0.0 (0.00)	0.0	0.00	0.00	323.80	1314.20
4	345	0.001	1882.85	0.4	2.2 (83.04)	0.0 (0.67)	0.0	22.98	8.78	323.80	2322.12
4	348	0.010	1364.97	3.4	2.0 (57.57)	0.2 (14.93)	0.2	268.98	29.47	323.80	2059.72
4	404	0.013	2402.15	9.6	11.5 (305.42)	0.5 (39.17)	0.3	243.18	112.06	323.80	3425.78
4	426	0.002	3268.07	1.7	3.1 (104.67)	0.1 (8.02)	0.0	16.92	16.61	323.80	3738.10
4	436	0.013	2302.55	10.4	4.4 (104.54)	0.1 (5.39)	0.2	205.15	42.29	323.80	2983.72
4	440	0.009	3270.36	5.2	7.9 (220.93)	0.2 (12.28)	0.1	97.03	46.49	323.80	3970.89
4	447	0.006	3985.64	12.2	13.8 (261.61)	0.1 (4.82)	0.0	28.77	48.68	323.80	4653.33
4	488	0.002	3561.96	1.7	4.5 (171.44)	0.1 (4.48)	0.0	29.01	40.00	323.80	4130.69
4	499	0.004	1535.80	3.9	6.3 (252.97)	0.5 (32.30)	0.2	192.35	72.32	323.80	2409.53
4	524	0.002	2785.31	1.7	2.1 (82.76)	0.0 (2.35)	0.1	48.60	16.31	323.80	3259.12
4	603	0.000	2889.68	0.1	0.8 (32.88)	0.0 (0.30)	0.0	8.85	4.92	323.80	3260.42
4	613	0.001	1428.24	0.3	0.2 (8.48)	0.0 (0.60)	0.0	14.16	6.60	323.80	1781.89
4	618	0.001	627.72	0.5	1.5 (56.85)	0.0 (2.26)	0.0	12.46	14.51	323.80	1037.59

PANEL	HMR	QOL LOST (QALY)	ANNUAL DRUG COSTS ($)	DAYS OF ILL HEALTH	NUMBER (COST, $) OF GP VISITS	NUMBER (COST, $) OF SPECIALIST VISITS	DAYS IN HOSPITAL	COST OF HOSPITALISATION ($)	COST OF PATHOLOGY INVESTIGATIONS ($)	HMR cost ($)	TOTAL COSTS ($)
4	676	0.001	2186.83	0.8	2.1 (73.25)	0.1 (3.49)	0.1	41.16	35.13	323.80	2663.66
	Total	**1.385**	**288211.66**	**806.7**	**573.8 (15875.29)**	**35.4 (2143.06)**	**33.5**	**33798.85**	**7528.35**	**38856**	**386413.22**

Appendix XXIII - Resampled incremental cost-effectiveness ratios

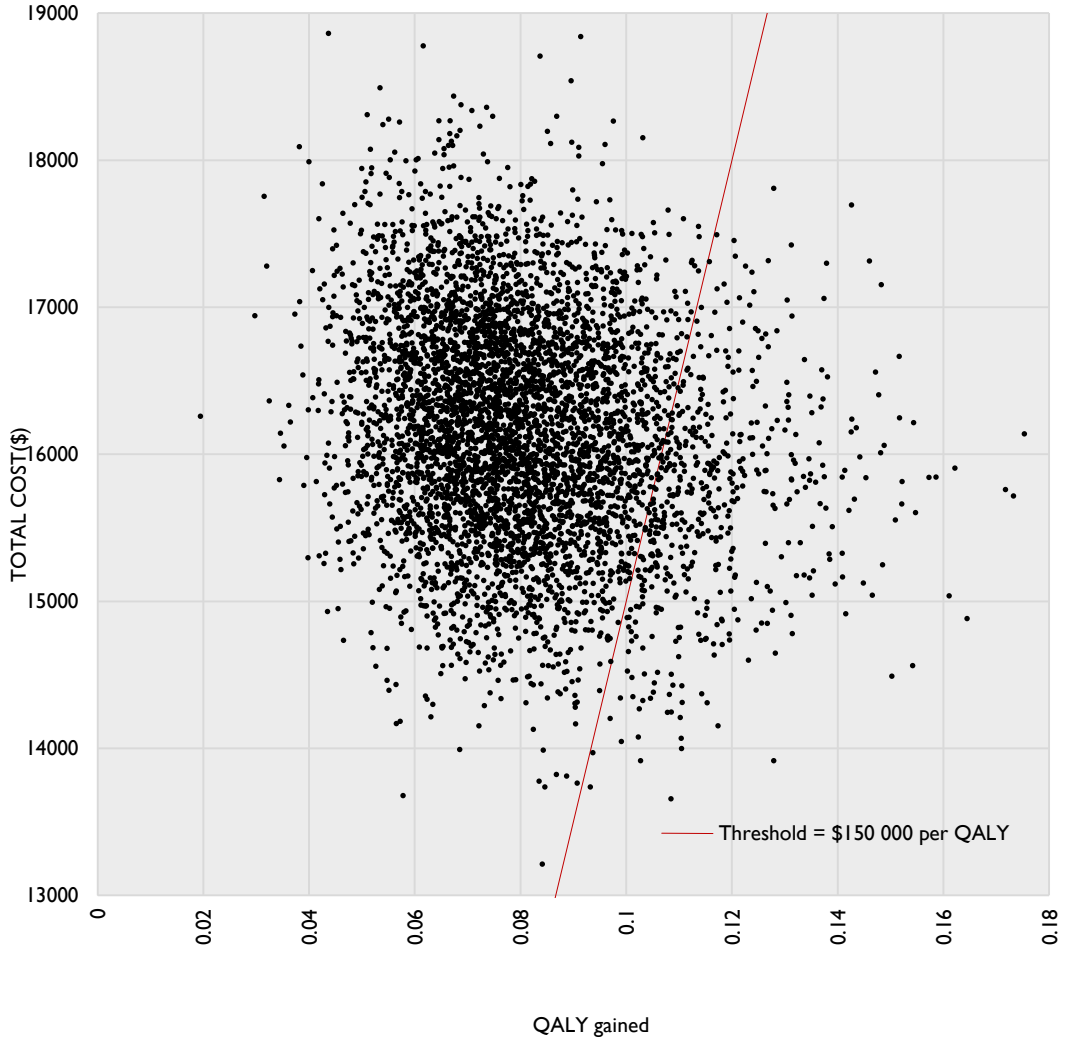

FIGURE 67 - RESAMPLED INCREMENTAL COST-EFFECTIVENESS RATIOS FOR HMRS VERSUS USUAL CARE: HMR COST INCREASED BY 10%

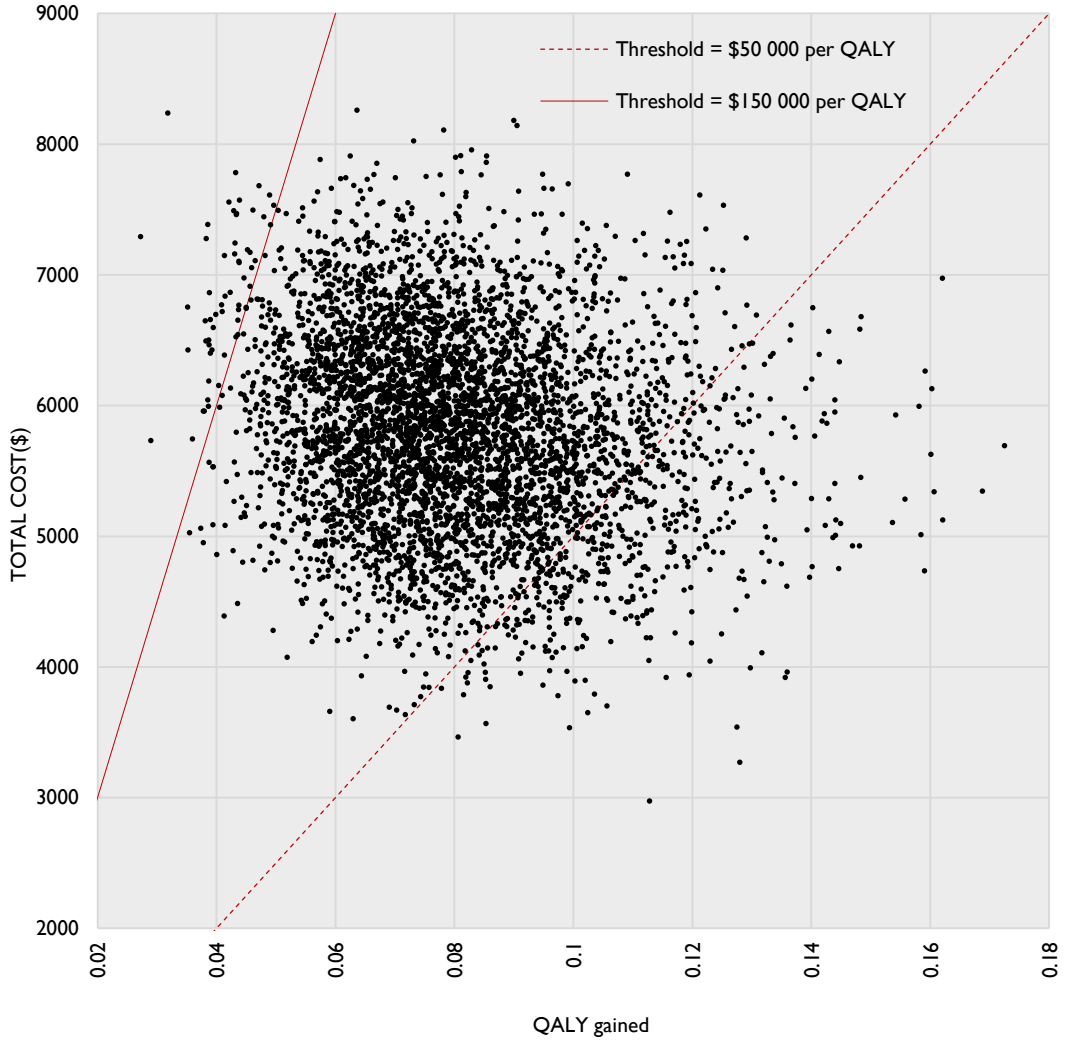

FIGURE 68 - RESAMPLED INCREMENTAL COST-EFFECTIVENESS RATIOS FOR HMRS VERSUS USUAL CARE: PHARMACY PAYMENT ONLY

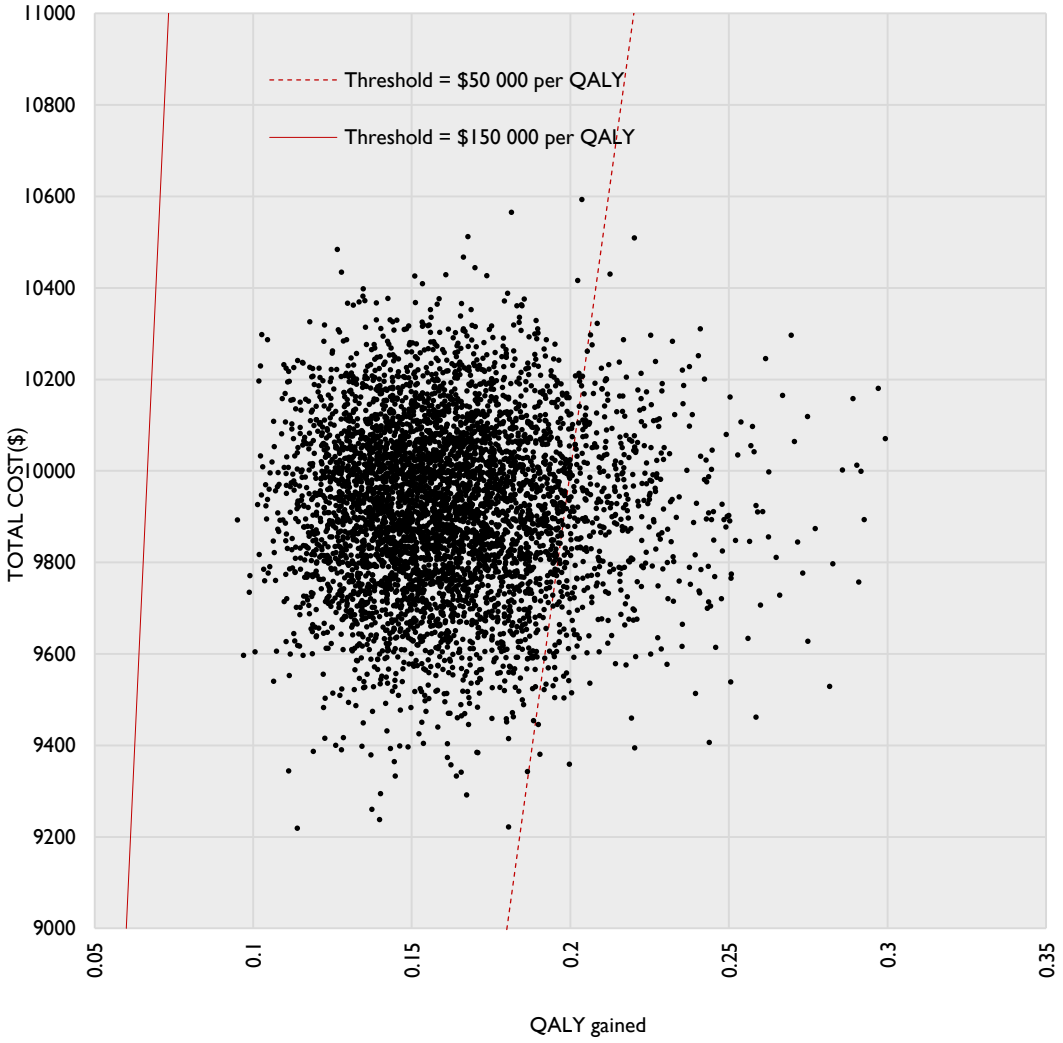

FIGURE 69 - RESAMPLED INCREMENTAL COST-EFFECTIVENESS RATIOS FOR HMRS VERSUS USUAL CARE: *ATTRIBUTION* COMPONENT REMOVED FROM MODEL

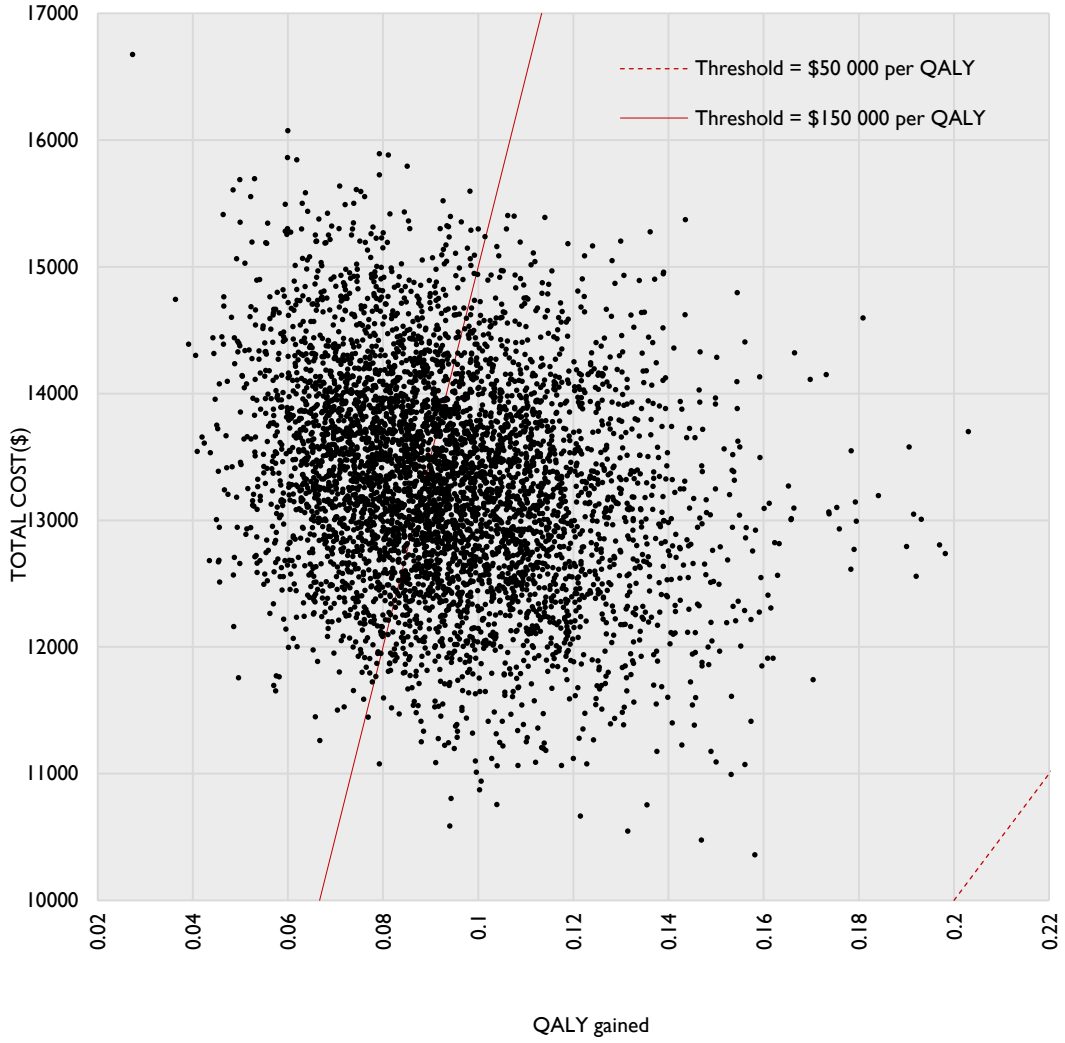

FIGURE 70 - RESAMPLED INCREMENTAL COST-EFFECTIVENESS RATIOS FOR HMRS VERSUS USUAL CARE: ASSUMES EVERY RECOMMENDATION MADE BY PHARMACISTS WAS ENACTED BY GPS.

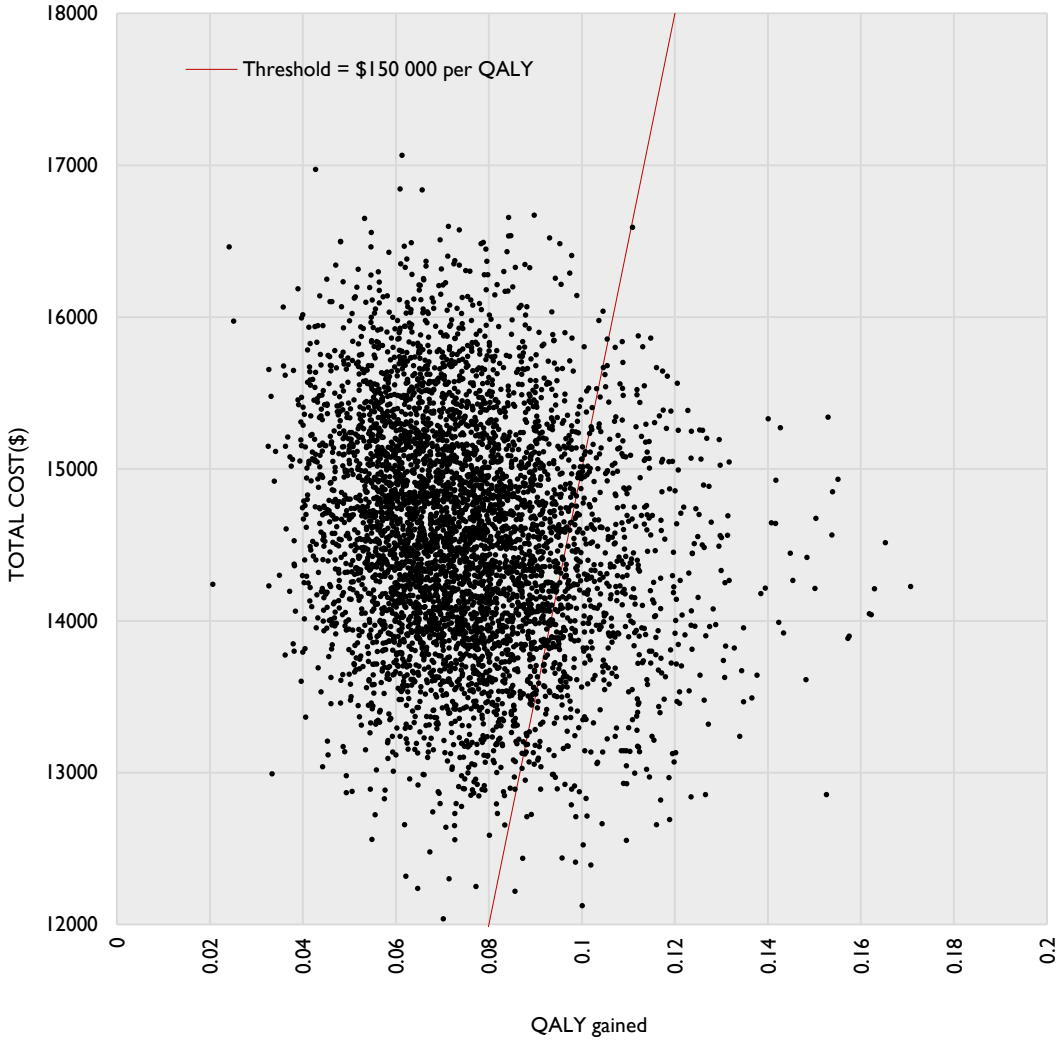

FIGURE 71 - RESAMPLED INCREMENTAL COST-EFFECTIVENESS RATIOS FOR HMRS VERSUS USUAL CARE: ASSUMES 42% PROBABILITY THAT RECOMMENDATIONS MADE BY PHARMACISTS WITH UNKNOWN OUTCOMES WERE ENACTED BY GPS.

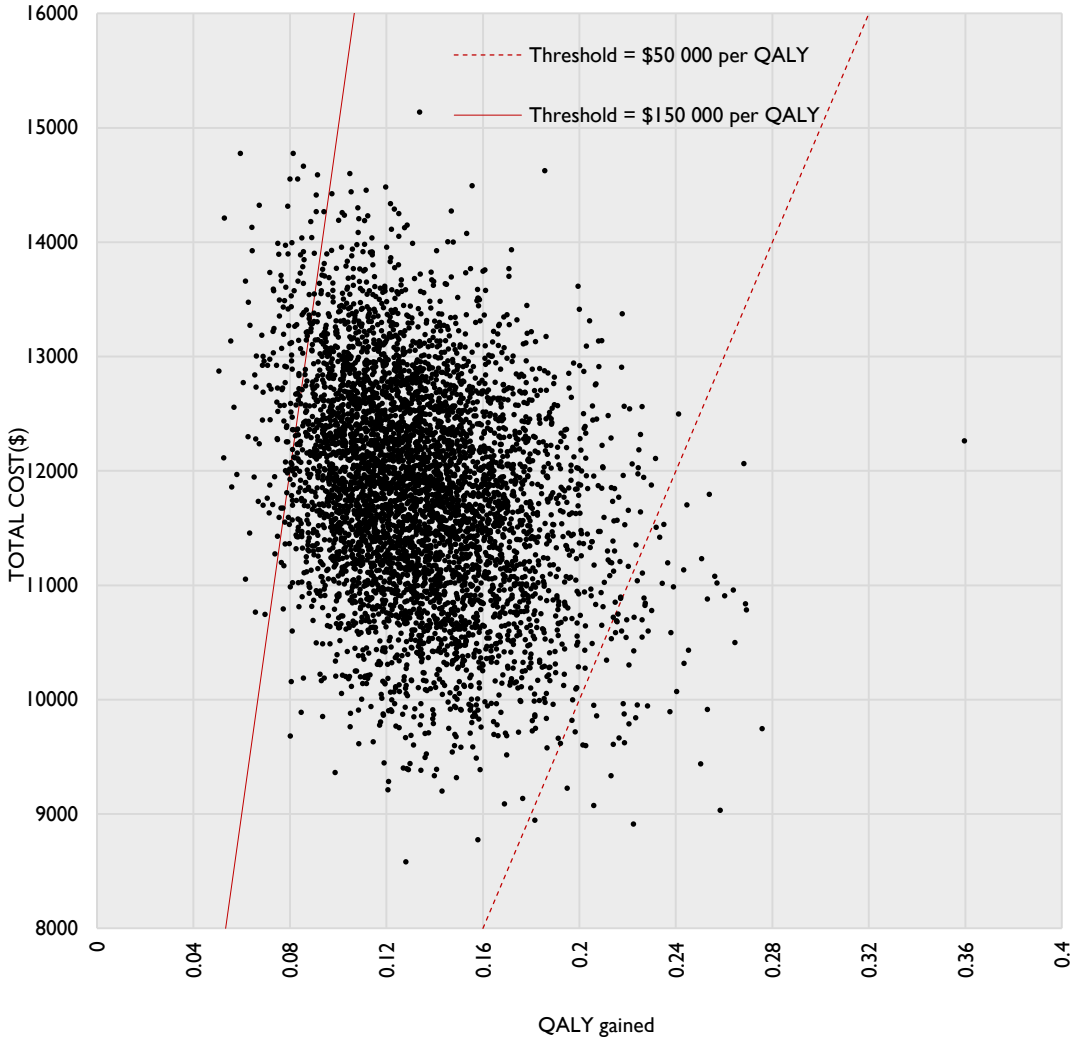

FIGURE 72 - RESAMPLED INCREMENTAL COST-EFFECTIVENESS RATIOS FOR HMRS VERSUS USUAL CARE: EACH ADDITIONAL DRP VALUED AT 100% OF AVERAGE DRP VALUE

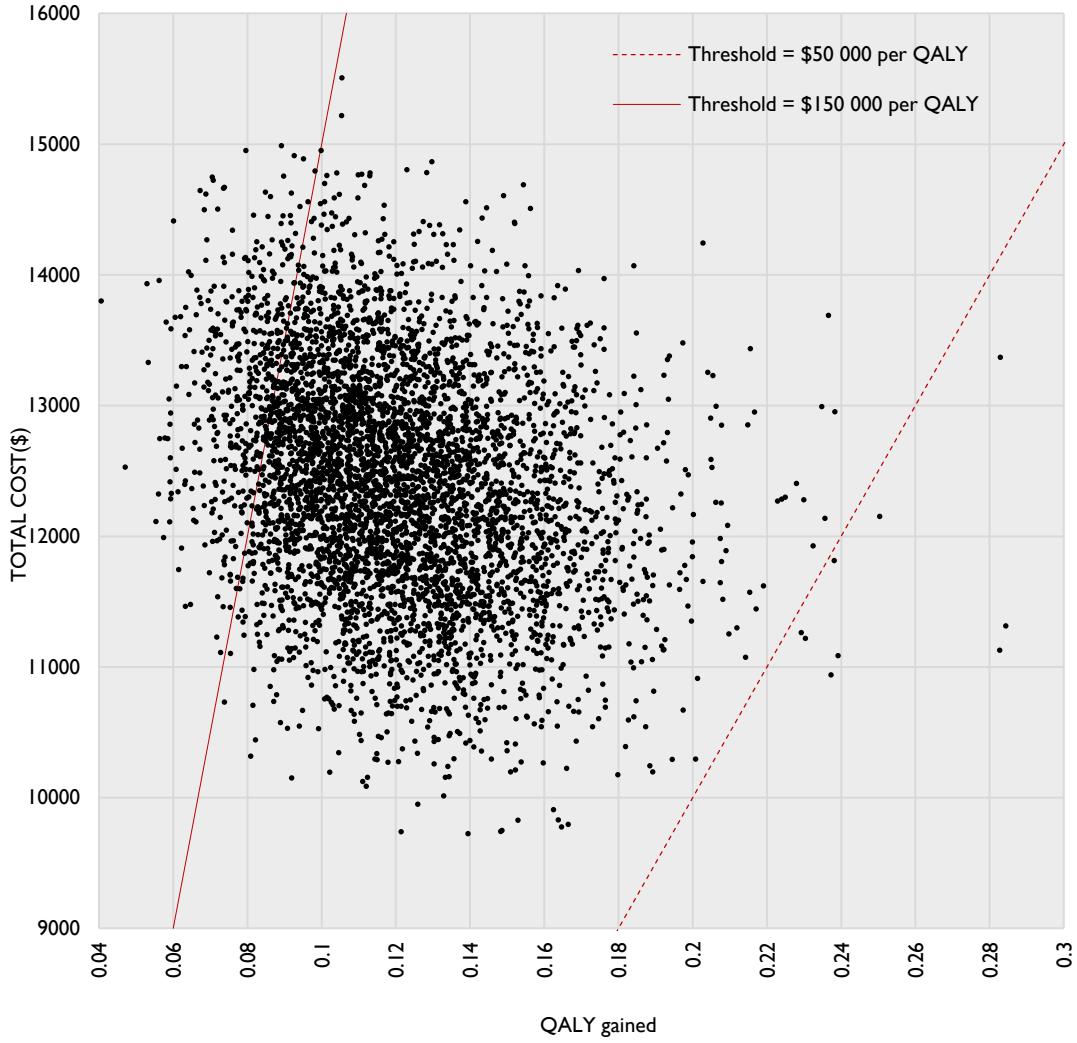

FIGURE 73 - RESAMPLED INCREMENTAL COST-EFFECTIVENESS RATIOS FOR HMRS VERSUS USUAL CARE: EACH ADDITIONAL DRP VALUED AT 75% OF AVERAGE DRP VALUE

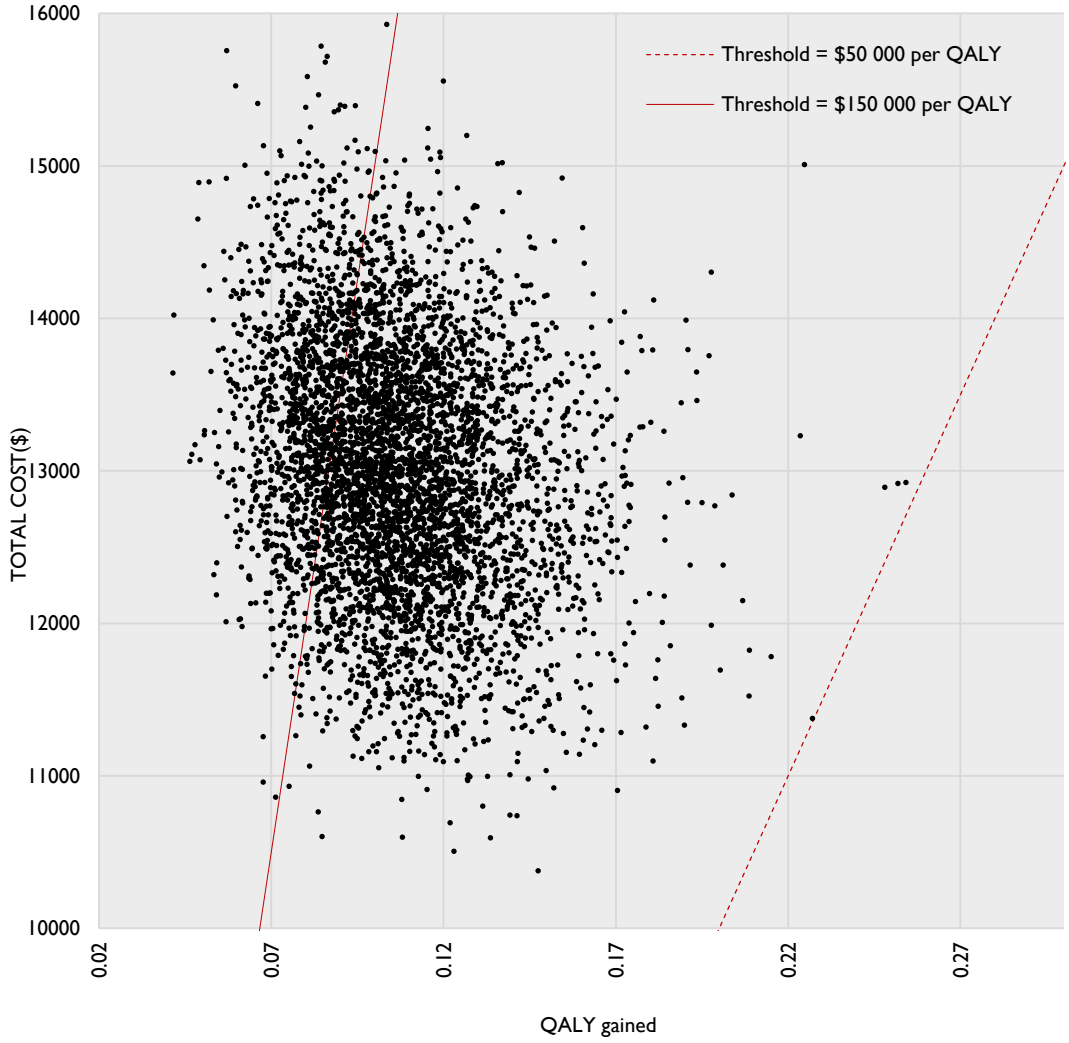

FIGURE 74- RESAMPLED INCREMENTAL COST-EFFECTIVENESS RATIOS FOR HMRS VERSUS USUAL CARE: EACH ADDITIONAL DRP VALUED AT 50% OF AVERAGE DRP VALUE

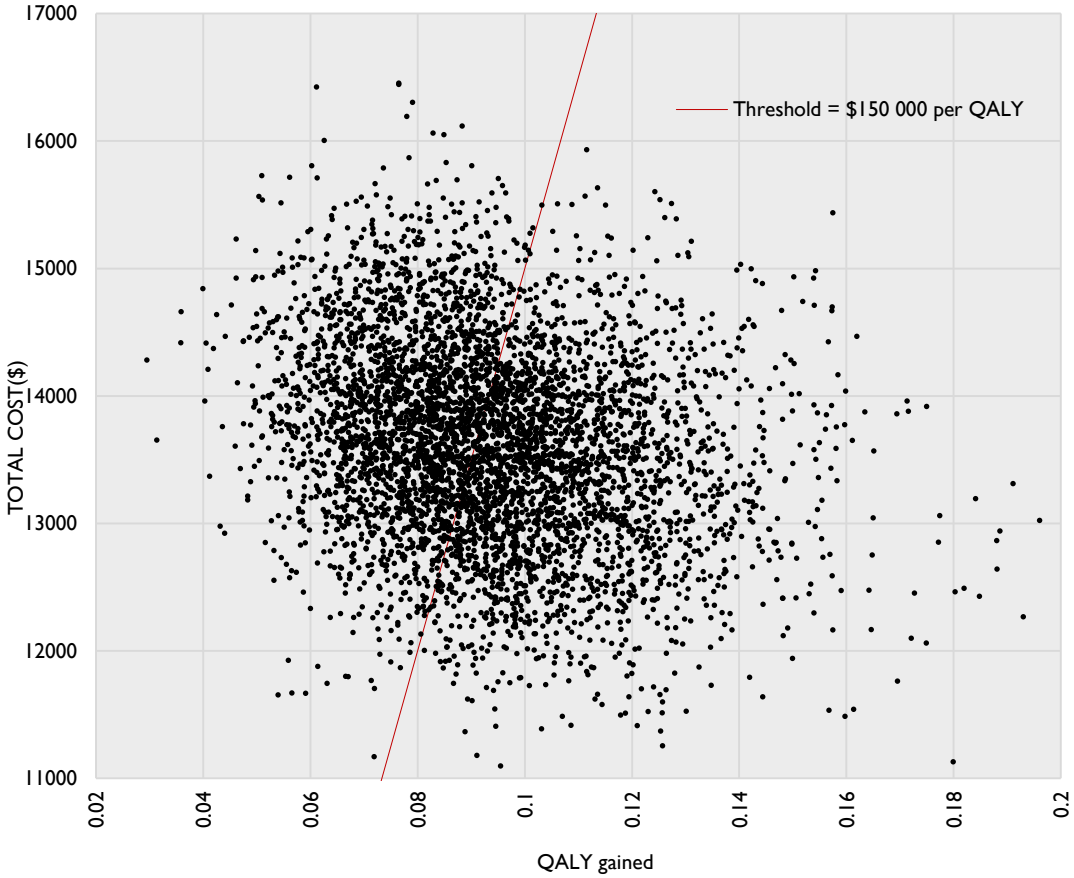

FIGURE 75 - RESAMPLED INCREMENTAL COST-EFFECTIVENESS RATIOS FOR HMRS VERSUS USUAL CARE: EACH ADDITIONAL DRP VALUED AT 25% OF AVERAGE DRP VALUE

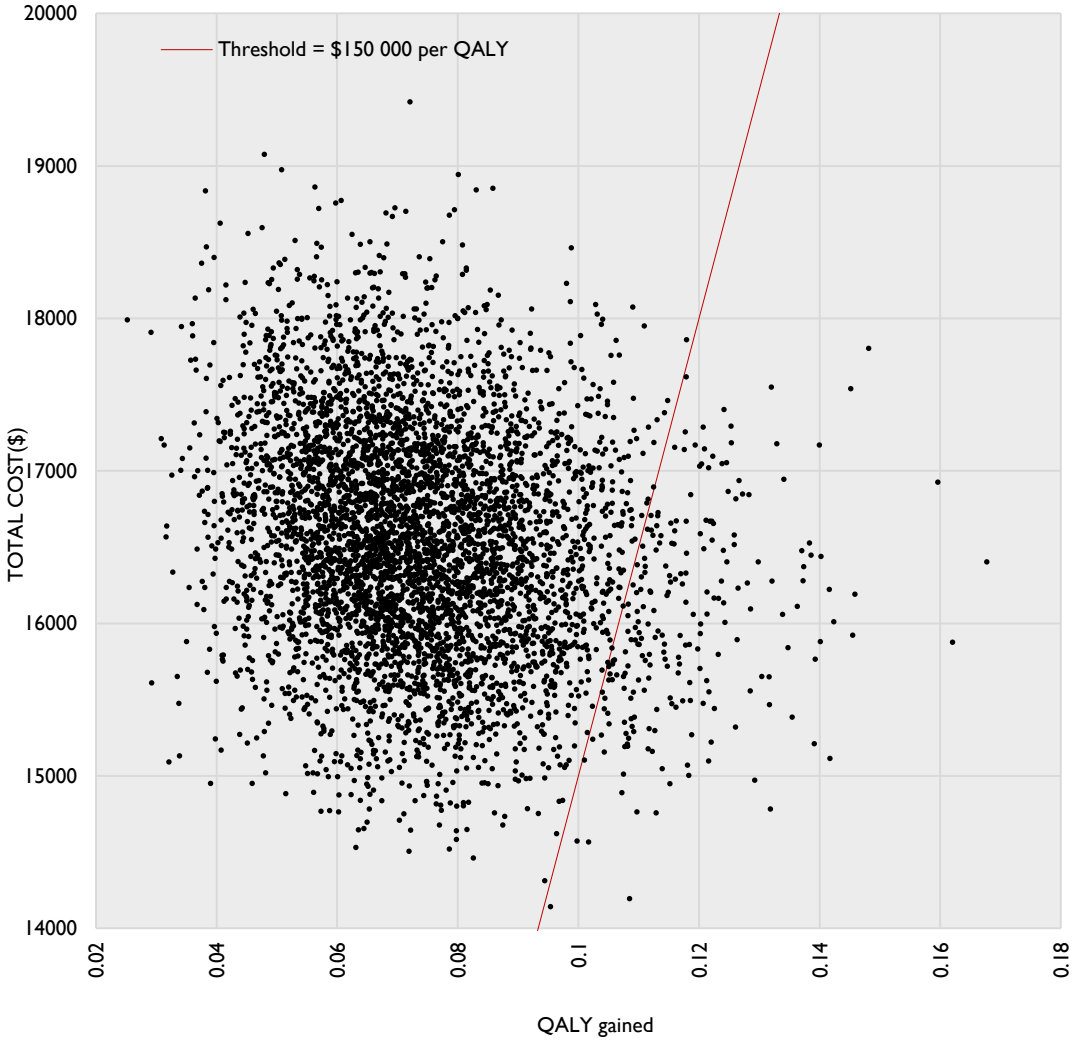

FIGURE 76 - RESAMPLED INCREMENTAL COST-EFFECTIVENESS RATIOS FOR HMRS VERSUS USUAL CARE: WORST CASE

Appendix XXIV - Comment from accredited pharmacist regarding provision of pathology/ laboratory data in HMR referrals

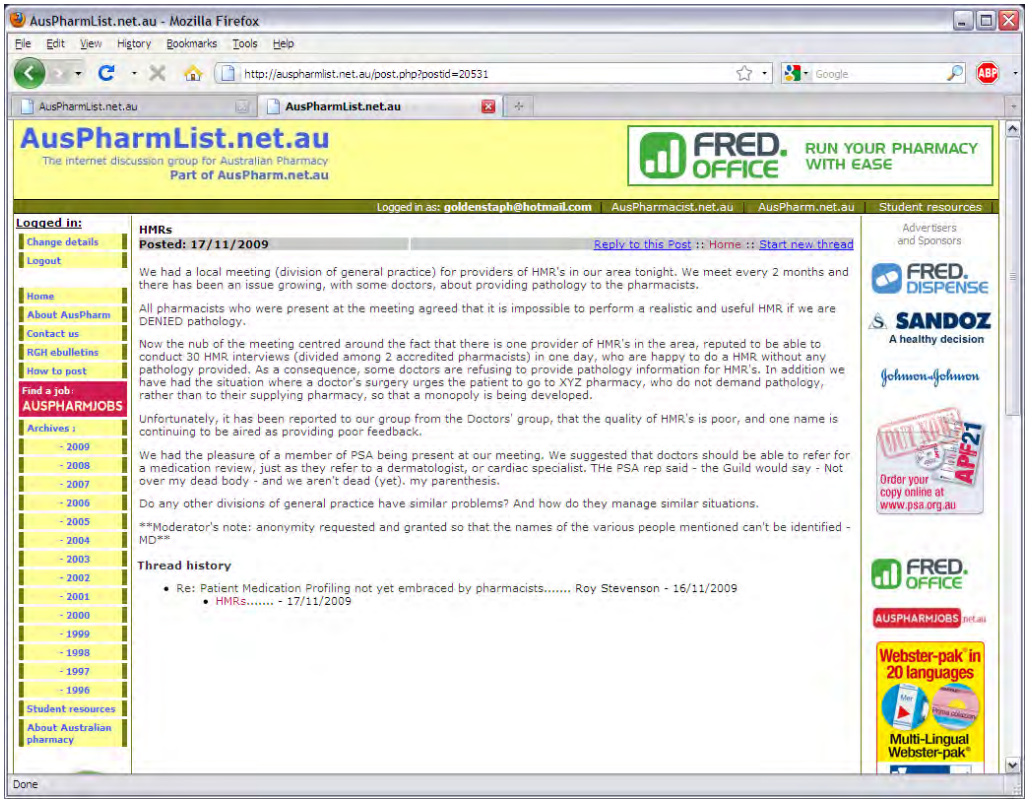

FIGURE 77 - POSTING BY PHARMACIST ON AUSPHARMLIST 17/11/2009
HTTP://AUSPHARMLIST.NET.AU/